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TUMOURS OF THE PALM AND SOLE RESEMBLING BASAL CELL EPITHELIOMA.

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TRUE basal cell epithelioma is rare on the sole and very rare on the palm. Pascher and Sims in 1954 reported two patients with such lesions on the soles. After a careful survey of the literature they were able to find only a single reference to the occurrence of such tumours on the sole and none describing them on the palms and this reference (Schreiner and Wehr, 1934) contained neither illustrations nor histological details. They stated that Beerman had studied one case histologically, but neither Montgomery nor Weidman could recall encountering such a tumour. Zugerman (1957) recorded another instance of basal cell epithelioma of the sole and said that Sachs had told him that he had seen six cases on this site. Gans and Steigleder (1957) mention only the patients of Pascher and Sims together with one which Rook (1950) presented at a meeting of the Royal Society of Medicine. This latter case had a rather Bowenoid structure in places and Rook has informed us that it later gave rise to metastases of similar type and so it probably cannot be classified as a true basal cell epithelioma. A relevant contribution is that of Pinkus *et al.* (1956) who reported lesions on the feet in five patients which they called "eccrine poroma" as they thought these arose from the intraepidermal portion of the sweat duct or acrosyringium. Two similar cases were reported by Knox and Spiller in 1958. Pinkus *et al.* described the acrosyringium as an entity distinct from the ordinary cells of the epidermis, consisting of "a well-defined diastase resistant cuticle, a layer of luminal cells and a single or multiple sheath of poral epithelium." The latter cells contained neither melanin nor tonofibrils and the nuclei often did not contain the large angular nucleolus usual in prickle cells, but showed several small chromatin masses. In addition, the cells of the acrosyringium contained glycogen and the cuticle stained with

P.A.S. They believed that histological examination of their tumours detected features strongly suggesting an origin from this structure.

We report two patients who presented lesions, one on the palm and the other on the sole, which on histological examination were first thought to be basal cell carcinomata. We now believe them to be similar to those described as eccrine poroma by Pinkus *et al.*

CASE REPORTS.

Case 1.—A man aged fifty-nine had had a lesion on his palm for about thirty years; he attributed it to an injury from a brick, soon after which a small lump had appeared and gradually increased in size. Examination showed a raised warty lesion 1 cm.

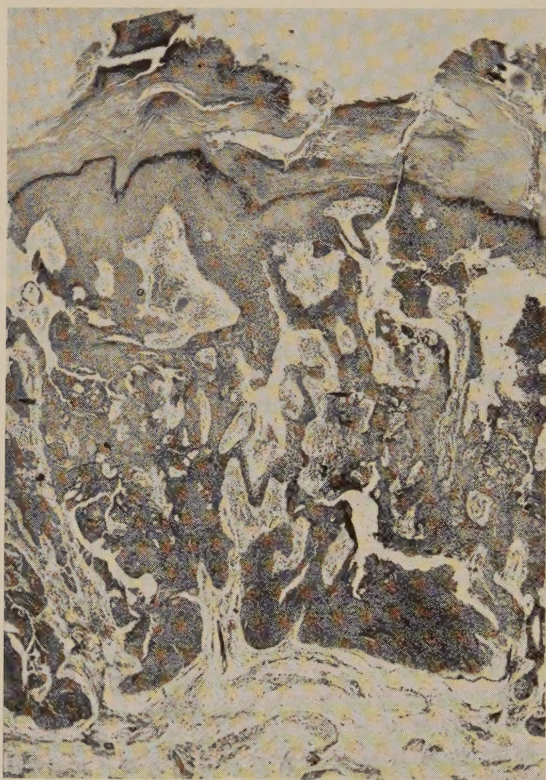


FIG. 1.

by 0.5 cm. on the left hypothenar eminence, surrounded by a keratinous collar. The diagnosis was uncertain but a foreign body granuloma was considered possible and the lesion was excised. When seen three months later the scar was sound and there was no evidence of recurrence.

Histological appearance.—The tumour arose from the epidermis multifocally over a considerable area and passed down into the dermis in interlacing columns (Fig. 1). There was an abrupt transition from the normal to the tumour cells. These

latter were round or oval and darker than those of the epidermis, with a distinct rim of eosinophilic cytoplasm; the nuclei were oval with scattered chromatin and a well marked nucleolus, though this was smaller and less conspicuous than that of the prickle cells. In other places the tumour cells showed darker, more spindle-like nuclei in which the exact structure could not be made out. The cells were arranged in whorls in some places and there was a faint tendency to form duct-like structures. The masses of tumour cells were not surrounded by any well marked palisade layer. The cells gave a positive reaction with P.A.S., most if not all of which disappeared after treatment with diastase, indicating glycogen.

Case 2.—A woman aged sixty-three. For two years she had had a lesion on the sole of her right foot which had been treated by a chiropodist. On examination there was an ulcer about 1.5 cm. in diameter under the outer side of the anterior part of the right heel, in the centre of which was some macerated whitish tissue. A provisional diagnosis of "overtreated plantar wart" was made and the lesion was treated conservatively with gentian violet lotion and protected. After temporary improvement, the ulcer failed to heal and persisted as a depressed rim with a macerated mass in the centre. A biopsy was performed and this specimen showed histological changes resembling those of a basal cell epithelioma. After consultation with the radiotherapist she was sent to a surgeon for excision of the tumour but she refused further treatment.

Histological appearance.—The tumour closely resembled the previous one, arising multifocally from the epidermis and extending downwards into the dermis in reticular fashion. There was a sharp transition between the normal epidermal cells and the darker tumour cells. These had elongated oval nuclei with ill defined scattered chromatin, a rim of eosinophilic cytoplasm and no intercellular bridges. There was no palisade arrangement of the cells surrounding the tumour masses. There was a considerable tendency towards the formation of ducts (Fig. 2); many of these were lined by a hyaline cuticle and closely resembled sweat ducts. There was a marked cellular infiltrate in the surrounding stroma consisting of plasma cells, lymphocytes and fibroblasts.

DISCUSSION.

In both cases the diagnosis was unsuspected until it was revealed by histological examination. This has been the experience of others; Pinkus mentions clinical diagnoses of pyogenic granuloma, fibroma, naevus and telangiectatic scar, whilst the possibility of amelanotic melanoma was considered in several cases. It should, however, at least be possible to suspect the correct diagnosis if one is aware of the condition. Knox and Spiller (1958) showed a picture of such a lesion and suggest that it might have a characteristic clinical appearance—the tumour protruding from a shallow, cup-shaped epidermal invagination. In our second case there was a very similar clinical picture which might have suggested the diagnosis had we been familiar with it. The progress of the tumour is slow, our first patient having had his lesion for thirty years and the other for two; and others have noted the same.

Pinkus believed that the tumours he described arose from the acrosyringium. He emphasised the abrupt transition from normal epidermis to tumour cells of rather smaller and uniform size and shape, with round or oval nuclei with dispersed chromatin and well developed intercellular bridges. He also noted

hypertrophic sweat ducts in association with three of his tumours and in others small clefts resembling the intraepidermal portion of an eccrine duct ; in several cases these were shown to be cystic differentiations within the tumour unconnected with normal ducts. The histological picture in our cases closely resembled the above except for the absence of intercellular bridges ; we also noted typical duct-like structures which were quite unconnected with any normal duct.

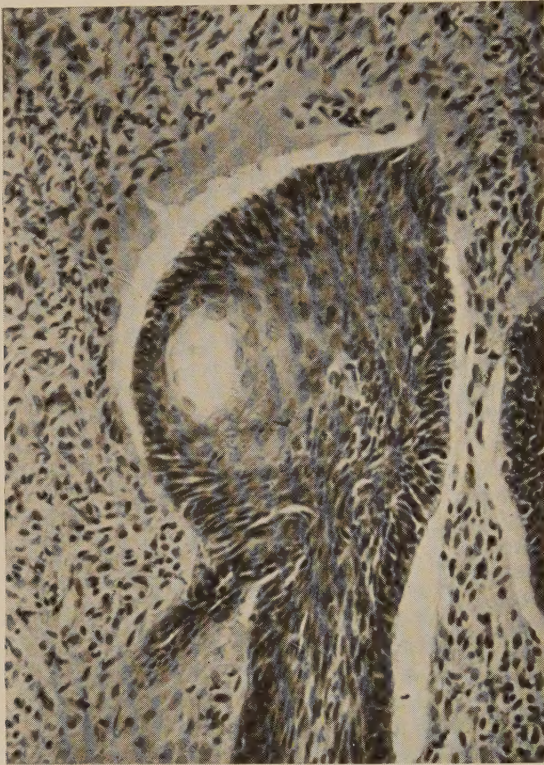


FIG. 2.

The question which most obviously arises is whether these tumours are a form of basal cell epithelioma or a separate entity. Arguments against the former are the presence of cells which are larger and paler than those of basal cell epithelioma and the absence of the palisade arrangement. Furthermore, Pinkus pointed out that "basal cell epitheliomas may contain considerable amounts of P.A.S.-positive material, but glycogen is absent almost regularly from the cells." In contrast, the cells of his tumours contained large quantities of glycogen ; we confirmed this in the case in which we looked for it. It seems highly probably therefore, that these tumours should be differentiated from

basal cell epitheliomas. They may be derived from the sweat gland apparatus, although we hesitate to say dogmatically that they arise from the sweat pore.

SUMMARY.

Two tumours, one on the palm and the other on the sole are described. Histological examination suggested that they were derived from the sweat duct apparatus and possibly from the acrosyringium as suggested by Pinkus.

The tumour may sometimes have a rather characteristic clinical appearance.

The lesions grow very slowly ; in one of our cases the tumour had been present for thirty years.

Dr. Hunter's address is now : 228, North Terrace, Adelaide, Australia. We would like to thank Mr. Hainsworth of the photographic department of St. James's Hospital, Leeds, for the photomicrographs.

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EPITHELIOMA FOLLOWING LICHEN PLANUS OF THE MOUTH.

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A SERIES of 45 patients presenting with lichen planus of the mouth has previously been reported (Warin, Crabb and Darling, 1958). Since this time 8 further cases have been seen. Amongst these 53 patients an epithelioma has by now developed on the inner cheek in two, on the tongue in one, on the lip in another, and two more have developed thickened plaques with clinical features and histological appearances of leukoplakia.

It has usually been taught that malignancy never develops in lichen planus of the mouth, but a gradually mounting number of such cases is being reported. Perin *et al.* (1950) found eight cases in the literature and described one more. In addition to these, Carteaud and Steigler (1950) and Marshal (1951) each described a patient and there are individual cases mentioned by MacKee and Cipollaro (1937) and Miller (1947), and Barker (1947) described two cases. There are therefore 15 reported incidents of epithelioma developing in lichen planus of the mouth, chiefly on the inner aspects of the cheeks and on the tongue. Most authors stress the importance of contributory trauma from sharp teeth, dentures or tobacco.

CASE REPORTS.

Case 1. A married woman aged 58, a housewife.

History.—The patient was first seen in 1949 when she had had a recurrent sore mouth and tongue for seven years. This commenced when she still had her own teeth which were later extracted, as sharp edges were chafing the sides of the tongue. Dentures had been worn since, but there was still some rubbing from these. Scattered spots on trunk and limbs had been present for two years.

Examination.—Superficial ulcers were present on the posterior part of the sides of the tongue, extending on to the dorsum and there was a similar ulcer on the upper posterior part of the right buccal mucous membrane. Over the anterior part of the dorsum of tongue there were white streaks and blotches and similar white streaks were present on the buccal mucous membranes and on the lips.

There were eight to ten papules on the back and lower legs suggesting lichen planus.

Investigations.—W.R. negative, blood count within normal limits. Histopathology: (i) papule on leg. Intense cellular infiltration consisting chiefly of lymphocytes, but separated from the epithelial rete. (ii) Tongue (non-ulcerated part). Hypertrophy with some downward growth of epidermis. Marked cellular infiltration with round cells in subepidermal layer.

Course.—She was given three doses of x-rays (150 r at 85 kV.) to the tongue and buccal mucous membranes but little change was noticed after this and during the the subsequent year. The ulcerated area almost healed at times but then enlarged again. She was not seen for four years and then in 1955 attended the radiotherapy

department for treatment of a growth starting at the site of the ulcerated area on the upper posterior part of the buccal mucous membrane. This growth was a typical squamous cell epithelioma clinically and histologically. It eroded the alveolar margin and palate and in spite of radiotherapy and surgery she died in June 1957.

Case 2. A man aged 68, retired engineer.

History.—The patient was first seen in September 1958 when he complained of a painful ulcer on the inside of the left cheek, present for six weeks.

Examination.—There was an ulcer with a hard raised edge, 2–3 cm. in diameter, in the centre of the mucous membrane on the left side of the mouth. Typical streaks of lichen planus and some annular lesions were seen on the buccal mucous membranes on both sides and on the lower lip. Small white patches of lichen planus were present on the edges and dorsal surface of the tongue.

Investigations.—The ulcer showed the typical histological picture of a squamous cell epithelioma. Blood W.R. negative.

Course.—The epithelioma was treated with radioactive cobalt and by block dissection of the cervical lymph nodes, but in spite of this the growth is still present and he is now having palliative treatment.

Case 3. A man aged 28, an insurance agent.

History.—The patient was first seen in 1952 when he gave a history of a sore area on the right side of the lower lip present for 4 months and gradually becoming more prominent. It was the area of his lip on which cigarettes rested. He smoked about twenty cigarettes a day. Ten years previously he had attended the same hospital with lichen planus of the skin but arsenic was not prescribed. Since this time he had noticed white areas in the mouth and on the lower lip particularly on the right side.

Examination.—There was a slightly warty infiltrated tumour 1 cm. in diameter on the right side of the lower lip. It was surrounded by white streaks and dots. White streaks were also present on the buccal mucous membrane with a small superficial ulcerated area on the right side. There was a patch of hyperkeratotic lichen planus on the front of the left leg.

Investigations.—The tumour showed the typical histological appearances of a squamous cell epithelioma.

Course.—The tumour was excised and he is at present well with no sign of recurrence.

Case 4. A man aged 60, a structural engineer.

History.—The patient was first seen in 1950 when he had typical lichen planus of the limbs, trunk and mouth. This cleared in six months; he was not treated with arsenic. In January 1957 he was seen again with a history that the tongue had been sore for five months.

Examination.—(January 1957). There were white patches and streaks on the right side of the tongue opposite the molar teeth and white streaks on the buccal mucous membrane. Sharp edges of teeth were impinging on the right side of the tongue.

Investigations.—Blood W.R. and Kahn negative.

Course.—The condition persisted and by August 1958 the patch on the tongue was much thicker and infiltrated. A biopsy specimen then showed the appearances of a squamous cell epithelioma. He was treated with radium needles and later underwent hemi-glossectomy and block dissection, at which time carcinomatous tissue was present in the lymph nodes. He is now receiving treatment for a further recurrence.

Case 5. A single woman aged 45, a clerk.

History.—The patient was first seen by me in February 1959. She had been under the care of Dr. R. Hadden and the history was that 5 years after a radical mastectomy for carcinoma, she developed lichen planus on the arms and legs and also had lesions in the mouth. The skin lesions improved, but new ones developed

and she had never been completely clear. In September 1958, she started to complain of a sore area on the posterior upper part of the inner right cheek, where the edge of her dentures was rubbing. A superficial ulcer developed in the raised white patch in this area. After two months, this was unchanged and a biopsy specimen showed the picture of leukoplakia with inward proliferation of acanthotic rete pegs and mitoses. This was treated with a radium implant.

Examination.—(Feb. 1959). At the site of the previously ulcerated area, the mucous membrane was red and thickened. Elsewhere over the inner cheeks there were numerous white streaks. On the outer aspects of the forearms and front of the right ankle, fading typical lichen planus papules were present.

Case 6. A married woman aged 47, a housewife.

History.—The patient was first seen in 1957, when she had noticed a white area on her tongue for 10 months with burning pain at times. The present dentures had been worn for twelve years.

Examination.—(1957). There was a white patch on the right side of the dorsum of the tongue and a white ring, dots and streaks on the buccal mucous membrane and on the dorsum of the tongue. She had ill-fitting dentures which amongst other defects, gave insufficient room for the tongue.

Investigations.—W.R. and Kahn negative. The thickened area on the right side of the tongue (1958) showed the histological appearances of leukoplakia.

Course.—The condition has persisted with periods when it is almost clear. The patch on the tongue has recently increased in size and has become more raised. At times sore areas have developed on the tongue.*

DISCUSSION.

Four cases out of 53 presenting with lichen planus of the mouth have developed squamous cell epithelioma and two more have a potentially malignant state. However, many of these have only been followed for a few years and in a large number the lichen planus is still present. It therefore seems likely that this rough incidence of 10% malignancy is likely to be higher when the cases have been followed up for longer periods. None of the six cases had been treated in the past with arsenic but four had evidence of irritation from teeth, dentures or tobacco at the site on which the epithelioma developed. Such factors are mentioned in many of the cases in the literature and it seems to be essential in cases of lichen planus of the mouth to remove any form of local irritation. Three cases have been described where epithelioma has developed on top of hypertrophic cutaneous lichen planus (Brennan and Teplitz, 1958; Wilson, 1953; Lyell and Whittle, 1951), but the trauma to these lesions must be considerable over the years. It is well recognized that there is a greater tendency for epithelioma to develop in the mouth. A number of authorities state that epithelioma can occur on top of lichen planus of the vulva. From my experience with lichen planus of the mouth, I would have expected this to happen, as superficial ulcers occur in some cases of vulval lichen planus similar to those seen in the mouth.

* In April, 1960, the lesion on the right side of the tongue became infiltrated and a biopsy showed the typical histology of an epithelioma.

SUMMARY.

During the past nine years 53 patients presenting with lichen planus in the mouth have been seen.

Four† have developed a squamous cell epithelioma, two on the inner surface of the cheek, the others on the tongue and lip respectively.

In two further cases, patches of leukoplakia have appeared.

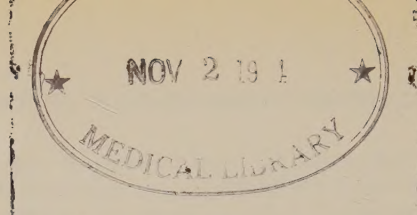
The importance is stressed of removing all trauma from sharp teeth, dentures and tobacco in these cases.

I would like to express my thanks to Professor A. I. Darling and Mr. H. S. M. Crabb, with whom I am associated in this work. I would also like to thank Dr. C. D. Evans for his help and interest and for referring cases to me.

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† See footnote.



KERATOACANTHOMA: A HISTORICAL NOTE.

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KERATOACANTHOMA has been the subject of numerous papers and reports since Rook and Whimster (1950) drew attention to its frequency and benign nature. It had previously been described by MacCormack and Scarff (1936), who called it "mollusum sebaceum". Later, Freudenthal coined the term "keratoacanthoma".

In their paper, Rook and Whimster commented on the lack of attention this rather common and characteristic affection had received in dermatological and pathological works. It would be surprising if it had not been previously observed and in the discussion aroused by the report of Rook and Whimster it appeared that a similar tumour had been described by Dupont (1930) with the name of "*kyste sebace atypique*" and by Gougerot (1929) who termed it "*verrucome*". Like mollusum sebaceum, these entities were nearly overlooked, though the absence of cases of *verrucome* described between 1931 and 1951 may have been due to Gougerot's insistence upon a satellite gland as an essential part of the condition, thus greatly limiting the number of cases.

Since it has been the fate of keratoacanthoma to be adequately described several times and equally often forgotten, it is of some interest to trace the history of this disease back to its first description.

On 2 April 1889, Jonathan Hutchinson read a paper to the Pathological Society of London entitled "The 'Crateriform Ulcer of the Face', a form of acute epithelial cancer" (Hutchinson, 1889). In the *Transactions* of that society, the paper is illustrated by a coloured plate showing three of the eight cases reported (Fig. 1). The description given there was later supplemented in a number of notes in Hutchinson's *Archives of Surgery*—the journal he wrote and edited alone—and by case reports in the *Clinical Journal* in the period 1894 to 1896.

The similarities between keratoacanthoma and the crateriform ulcer of Hutchinson are immediately apparent from the first paragraphs of the paper.

"The form of malignant disease which I have to describe differs very widely from what is known as rodent ulcer, although it occurs on the same parts and under very similar conditions. It is a disease of very rapid growth, whilst rodent ulcer is well known to be very slow, and it produces appearances very different indeed from rodent, and I think from all other varieties of cancer hitherto described. I have for many years been in the habit of calling it the 'crateriform ulcer,' a name more or

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FIG. 1.—Hutchinson's "Crateriform Ulcer of the Face" (*Trans. path. Soc. London.*, 1889, 60, Plate 25).

less appropriate on account of its taking on the form of a large elevated boil (or a beehive), and then breaking down into a deep hollow in the centre."

"The growth . . . begins as a painless papule . . . and in the course of a few months lifts itself to the height of a quarter or half an inch or more. Its base is rounded and usually, but not always, well defined and free from inflammation. At the end of a few months a process of breaking down begins in the centre, and a large cavity is excavated. At all stages the substance of the growth, although not hard, is very firm.

"A very remarkable feature in the disease, and one which is especially so when we take it in connection with its rapid development in the first instance, is that the disease after excision does not appear to be prone to recur." "I have never seen the glands enlarged, but then I have not watched some of my cases for very prolonged periods." (Hutchinson, 1889.)

The decisive observation of the relatively benign character of the crateriform ulcer was confirmed seven years later when he "drew attention to the very important feature of these acute epithelial ulcers—that they appear to have little infective power, and do not recur after free excision, nor do they, so far as I have observed, infect lymphatic glands early." (Hutchinson, 1896a.)

A summary was given in a short note in the *Archives of Surgery*, and I cite it in full because of the precision of the description.

"The ulcer is an acute form of epithelial cancer, which occurs on the face, much in the same position as rodent does. It occurs also at the same ages and in the same class of patients as rodent. Its features and clinical course are, however, quite different from those of rodent. It makes as much progress in weeks as rodent often does in years. It is indeed one of the most rapidly growing forms of malignant disease with which I am acquainted. Its development is very peculiar and exactly alike in all cases. It begins as a red, firm tubercle, which involves the deeper parts of the skin, and rapidly develops into an elevated mass shaped like a beehive; this soon breaks down in the centre, and produces the condition which is denoted in the term 'crateriform'; there is very little inflammation at the base, the surrounding skin remaining quite sound." (Hutchinson, 1890.)

"The amount of breaking down in the middle is but small and the progress slow, so that no condition of a hollow with overhanging edges such as is often seen in other forms of disease, is ever produced. The only condition under which they are at all simulated are in certain forms of syphilis." (Hutchinson, 1891-2.)

Hutchinson thought the difference between rodent and crateriform ulcer to depend "in all probability upon difference in the precise structure in which the malignant action begins. Rodent cancer is now generally acknowledged to commence by growth in the rete, whilst (presumably) the crateriform ulcer may begin in gland structures." (Hutchinson, 1895a.)

The pathology of the lesion was described in the original paper and in more detail in connection with a later case report. "The specimen consists of tissue so arranged as to give the aspect of a squamous-celled carcinoma. The tumour is remarkable for want of surface-hypertrophy of epithelium. The epithelium passes from the flat surface, where it is still comparatively normal, over a rounded elevation where it becomes gradually thinned out. The elevation is caused by proliferation of the connective tissue elements and round cell exudation. Through this mass of tissue are scattered masses of epithelial cells arranged in a manner characteristic of the deeper prolongations of a squamous carcinoma. On advancing farther into this tumour-like mass, its surface epithelium becomes more thinned out, while the deeper prolongations of epithelium become more pronounced. Epithelial 'cell nests,' characteristic of overgrowth of squamous epithelium, make their appearance.

"On passing over the edge of the rounded tumour surface epithelium disappears, the surface being covered simply by a thin fibrous membrane—resembling a thickened basement membrane. The surface shows small collections of exudation in position. Gradually this surface membrane disappears and the exposed connective

tissue surface is evident. Projecting into the deeper structure from all parts of this denuded surface are the prolongations of epithelium already described." (Hutchinson, 1896a.)

The pathological report is consistent with a keratoacanthoma. The original specimens cannot be traced, since the Hutchinson Collection in the Museum of the Royal College of Surgeons was lost during the fire in 1942.

As witnessed by the number of references, Hutchinson rather persistently returned to the crateriform ulcer. He showed a drawing of it at the Third International Congress of Dermatology in London in 1896 and a further plate was published in the *Archives of Surgery* showing two cases found by Hutchinson after a systematic search through the collections of the Hôpital St. Louis (Hutchinson, 1897). One of the latter cases is described as "typical" and indeed seems a typical keratoacanthoma, the other "less so".

The concept of the crateriform ulcer survived for little more than a decade. A few cases were presented at meetings of the Dermatological Society by other members, the first in 1889 by Anderson from St. Thomas's Hospital, the last in 1898 by Radcliffe-Crocker, who also mentioned crateriform ulcer in his text-book (1903), though with the comment that nearly all the cases he had seen had developed on a previous rodent ulcer. Other text-books from this period either ignore the term or employ it as a morphological description.

Hutchinson was therefore again responsible for the first description of a dermatological entity, although this one was forgotten for many years.* It is interesting that he also recognized that the lesion did not recur after excision, or show evidence of malignancy other than the suggestive histological changes.

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* Prof. J. T. Ingram, in his Presidential Address to the Dermatological Section of the Royal Society of Medicine on 17 October, 1957, drew attention to the picture in *Illustrations of Clinical Surgery* in which "Hutchinson shows a beautiful example of kerato-acanthoma of which he had seen many cases. He thought it was an epithelioma but stressed the very short history and the good prognosis. But he excised and did not therefore observe spontaneous recovery."—EDITOR.

ENDOXAN ALOPECIA.

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ENDOXAN (N,N-Bis (β chlorethyl)-N¹, o-propylene phosphoric acid ester diamide), is a cytostatic substance, in which nitrogen mustard is neutralized by an electronegative phosphoryl group. (Arnold *et al.*, 1957 ; Pfeiffer, 1958 ; Brock, 1958). The transport form so constructed is used in the chemotherapy of malignant disease.

In 1958 Gross and Lambers first reported loss of hair in 2 of 62 cases treated with Endoxan. There appear to be no other reports of alopecia in man from Endoxan and histological studies of the affected areas are lacking. No reports of Endoxan alopecia in animals have come to our notice. In our experience of this drug during 1959, alopecia followed its use in 10 of 25 patients treated for serious malignancies. Had there been more survivors in this group under treatment, alopecia might have been seen even more often.

Endoxan is relatively less toxic to leucocytes than other cytostatic drugs and its cytostatic activity is measured *in vitro* by its inhibiting action on the enzyme phosphoglyceraldehyde dehydrogenase. (Löhr, 1957). Alopecia has been shown to result experimentally from non-inflammatory inhibition of various enzymes of the hair roots, (Braun-Falco and Theisen, 1959) and this represents one possible mode of action of Endoxan, although sulphhydryl groups do not appear to be primarily involved. Mitotic poisons (colchicine, triethylene melamine, certain triazine compounds etc.) are also known to produce alopecia (Strauss and Kligman, 1954). Two mechanisms may be responsible here—first, mitotic inhibition of the hair root, which is one of the most active sites of cell division in the body, and second, cell disintegration from higher concentrations of the antimetabolic substances. How Endoxan in fact destroys the hair follicle cannot be stated, but the histological findings presented here emphasize the importance of cellular disintegration.

CLINICAL FEATURES.

Table I shows the race and sex distribution in our series of cases treated with Endoxan. In Table II the clinical and therapeutic data in the alopecia group are set out. Fig. 1 shows the clinical appearance in Case 1. By comparing the findings in Table I and II with those (not presented here) of the 7 patients

who survived more than 1 month and did not develop alopecia, the following conclusions were drawn.

The alopecia could not be correlated with the dosage of Endoxan, its influence on the white cell count or with Röntgen therapy. Both Endoxan and Röntgen therapy were given to several cases who developed no alopecia and marked granulocytopenia was not followed by loss of hair either. The younger white



FIG. 1.

women patients tended to have more severe alopecia. In three out of ten cases the marginal scalp hairs were better able to resist the epilating action of the drug. In no instance were eyebrows or eyelashes affected. This resistance is seen also with other diverse epilating drugs (Rothman, 1955). In two patients

TABLE I.—*Age and Sex of 25 Cases Treated with Endoxan.*

Sex.	Race.	Number of cases.	Number with alopecia.	Number dead 1 month after treatment.
Female . .	White . .	8	7	1
Male . .	„ . .	4	1	1
Female . .	Bantu . .	2	1	1
Male . .	„ . .	11	1	5
Totals . .		25	10	8

TABLE II.—*Details of Patients with Endoxan Alopecia.*

Age. Case. (yrs.)	Race.	Sex.	Disease.	Special features.	E.	T.	A.	B.	Regions affected by alopecia.	Course of alopecia.	White cell count (cu. mm.).	Response of disease.
1	White	Female	Hodgkin's disease	Severe laryngeal compression	2,000	1	2½	2½	Scalp, diffuse, worse on vertex and parietal areas	Little improve- ment in 3 months	Unchanged	Radiotherapy. Superior media- stinum 3 days before En- doxan.†
2	41	"	Carcinoma of breast	Severe jaundice. Liver, bone, lung metas- tases. Critically ill	5,600*	4	3	2	Scalp, diffuse, worse on crown	Remains mild	10,000 to 3,000	Radioactive gold in pleural cavity 3 weeks before Endoxan.
3	60	"	Carcinoma of gall bladder	Diffuse liver me- tastases	5,500	4	2½	—	Scalp and body hair	—	60,000 to 3,000	Poor relief of pain for one month
4	43	"	Carcinoma of cervix uteri	Metastases. Con- stant pain	2,200*	1½	3½	3	Mainly temporoparietal. Con- currently, first attack of severe dermatitis seborrhoic	Decreasing	20,000 to 2,500 to 1,400 (86% polys.)	Fair relief of pain None for 2 years.
5	69	"	Hodgkin's disease	Abdominal lymph glands causing acute symptoms	2,400*	2	10	—	Scalp, mild insi- dious diffuse	Increasing with oral Endoxan	10,700 to 5,200	Good remission. Complete symptomatic relief
6	54	"	Carcinoma of breast	Diffuse bone metastases	6,000*	4	3	—	Scalp patchy	Regrowth des- pite oral En- doxan	11,000 to 4,000	Very good. Sub- jectively and objectively im- proved
7	72	"	Carcinoma of gall bladder	Diffuse liver infiltration	4,000*	3	3	7	Scalp, slow with special thinning in parietal area	Remains rela- tively mild	10,000 to 4,500	Good. Weight increase.
8	31	Male	Chronic myeloid leukaemia	—	40,000*	22	20	—	Scalp, generalized thinning	Mild and tran- sient	60,000 to 4,000 (5-70% blasts and immature cells)	Asymptomatic Poor. Subacute leukaemia 16 weeks after starting En- doxan
9	30	Bantu Female	Ditto	Splenomegaly, purpura, lym- phadenopathy	14,000*	12	12	12	Aggravation of traction alope- cia at edges of tight tribal hair plats	—	400,000 (12% blasts, 50% polys) to 10,000 (3% blasts, 58% polys.)	Good improve- ment. Slowly attained
10	60	Male	Chronic lymphatic leukaemia	Gross lymphatic adenopathy	12,000*	4	3	7	Diffuse on scalp, beard, axillary and pubic areas	Regrowth des- pite oral En- doxan, 15,000 mg. over 4 weeks	60,000 (76% lymphos.) to 4,800 (36% lymphos. No further change with oral dose	Very good. Sub- jectively and objectively well

E : total dose of Endoxan in mg. given intravenously. T : time over which Endoxan was given in weeks. A : time of onset of alopecia in weeks after starting Endoxan.
B : time of scalp biopsy in weeks after onset of alopecia. * continues with oral maintenance therapy. † X-rays given to superior mediastinum, skin area 10 cm. by 15 cm., total skin dose 100r given once 3 days before Endoxan was started. Factors : 220 KV, 50 F.S.D., 16 mA, Filter 1 Cu, 1 Al.

(Cases 1 and 8) the alopecia started after the patient had become critically ill. Alopecia usually became noticeable at about the third week after Endoxan was first given, but sometimes this was delayed in the milder cases till about the second month. Though it varied greatly in rate and amount, regrowth of hair was invariable after stopping Endoxan.

Both Bantu patients (Cases 9 and 10) developed a dusky melanosis spreading up the proximal half of the nailplates of all the fingers during Endoxan treatment.

HISTOLOGICAL FEATURES.

Cases 1, 2 and 4 showed the earliest changes seen in the scalp in our series.

The basal and malpighian epidermal cells were shrunken, reduced in numbers and non-mitotic. Their cytoplasm was sparse, granular, fibrillar and sometimes vacuolated and the cell nuclei condensed. The basal and suprabasal cells had often retracted from one another or from the basement membrane, thus creating spaces which trauma during biopsy may have aggravated. Clinically there was no evidence of epidermal separation. The folded or polypoid dermo-epidermal junction showed

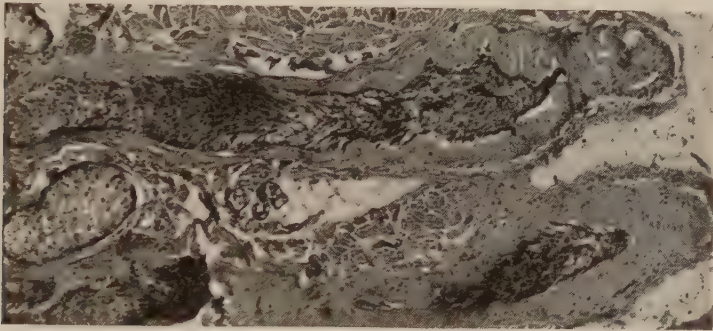


FIG. 2.

some small dentate projections where the feet of the basal cells had lost their moorings and the spaces contained a little fibrillar and granular detritus. Similar changes occurred down the follicles—a loss of cell numbers and substance, retraction of the outer root sheath from the follicle wall and a gathering up towards the surface of the collapsed perifollicular tissue (vitreous membrane and connective tissue sheath) which became thick and folded in the process (Fig. 2). In one specimen where a few coarse hairs were still retained, the same oedematous and fibrillar disintegration affected the hair shaft and its root sheaths just above the bulb.

In the other specimens, all inner root sheaths, hair and bulb structures were gone, leaving only some melanin debris scattered in the surviving follicular cells. The sebaceous glands were small to moderate in size with increased cytoplasmic granularity between the fat droplets. The sweat gland acini showed degeneration of the secreting cells and disorganization of their arrangement, to the point where only the periaccinar hyaline ring survived or the gland relics were quite unrecognizable. The dermal connective tissue showed variable oedema with possibly some granularity and pyknosis in the pericapillary and fibroblast cell bodies. The fat seemed unaffected and the arrector pili muscles were unchanged except for being broad and bunched up when unattached to identifiable follicular structures.

Cases 2 (repeat biopsy). 7, 9 and 10 showed changes suggesting regeneration. The epidermis was only a few layers thick and the cells showed solid cytoplasm with some remaining perinuclear vacuolation. Undifferentiated cellular downgrowths and the formation of small new hair bulbs, papillae and sometimes hairs was noted. The connective tissue and epidermis throughout gave a compact, nonoedematous and sharply staining picture. Some follicles still showed melanin clumps which were thought to be the residue of the previous hair, caught up in the regrowth.

COMPARISON WITH OTHER CHEMOTHERAPEUTIC AGENTS.

(i). *5-fluorouracil* is an antimetabolite from which alopecia is said to occur in 10% of cases treated (Ansfield, 1958). There are no published histological studies concerning it. We have had eleven cases under constant observation who have had repeated courses of 5-fluorouracil without any of them losing hair.

(ii). *Triethylene melamine*, despite extensive use, has caused no alopecia in our cancer patients.

(iii). *Actinomycin-C* has caused alopecia in one of our cases. The side effects of this cytostatic substance include changes suggesting interference with the metabolism of the vitamin B complex, particularly pantothenic acid (Martin, 1954). Our case showed an histological picture in no essential way different from that produced by Endoxan and the clinical resemblance was equally close.

(iv). *Carzinophilin*. None of our cases treated with this preparation showed any hair changes.

DISCUSSION.

Although X-rays can produce alopecia in the shielded animal in a parabiotic experiment i.e. in the non-irradiated animal (van Dyke and Huff, 1942), and although it is accepted that Endoxan is potentiated by Röntgen therapy, we find no reason to believe that the alopecia in our cases was aggravated by X-ray therapy. None of our patients received Röntgen therapy to the head or neck at any time. The wrinkling and thickening of the vitreous membrane as seen in our sections is described after irradiation. (Montagna and Chase, 1956; Kligman, 1954). Although we have not been able to perform serial biopsies on our cases the histological features suggest that the action of Endoxan on the epidermal derivatives is largely radiomimetic.

SUMMARY.

The histological appearance and clinical significance of alopecia occurring in patients receiving Endoxan therapy are described. Attention is drawn to the high rate of occurrence—10 out of 25 patients treated to date being significantly affected.

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ERUPTIVE TELANGIECTATIC CELLULAR NAEVI.

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CELLULAR naevi can appear suddenly, but it is rare for them to do so simultaneously in sufficient numbers to justify the description eruptive. *Lentiginose profuse*, the term introduced by Darier (1902) and used since from time to time in the French and German literature, stresses the abundance and widespread distribution of the lesions rather than their abrupt onset, which was striking in several of the reported cases. This type of onset separates these cases from those of generalized lentigo such as were described by Zeisler and Becker (1936) and Fisher (1951) and from the not uncommon cases of disseminated pigmented cellular naevi. It is probably in the last group that the case described by Hutchinson (1868) belongs.

Darier's original case, briefly reported with a photograph in *La Pratique Dermatologique* (1902), was that of a girl, aged 6 years, who broke out in innumerable spots following an attack of German measles. These were yellow at first and darkened to brown or black. The mucous surfaces were not affected and her health was perfect. Biopsy of the lesion showed the typical structure of lentigo. The patient was reviewed at the age of 22 and the disease was stated to have diminished progressively, many of the black spots having disappeared and others, notably those on the forearms, remaining only as small and less obvious macules.

The case which Balzer, Gaucher and Milian (1897) described as *lentigo mélanique* was considered by Darier to be an example of the same disease as the one he described. In this patient, a girl of 29 years, the lesions appeared suddenly while she was convalescing from typhoid fever. They were disseminated brown spots, confluent on the backs of the hands and fingers, pin-head to lentil sized, round or oval, and varied in colour from *café au lait*, through sepia to indian ink. The arrangement of the lesions was said to be like that of xeroderma pigmentosum. The histological description leaves room for speculation, but is in keeping with that of a cellular naevus.

Dumas, Petouraud and Benoit (1933) described the case of a 58-year-old woman who, eight months before, had developed an eruption of lentil-sized light brown spots on the trunk, arms and thighs. These spread profusely, becoming almost confluent on the flanks and axillary regions. The lesions were

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round, not raised, with skin of normal consistency beneath them and with no scaling of the surface. They did not follow a different-looking eruption. There was also itching and urticaria, but the authors considered these to be separate manifestations. There is no record of the histological appearance. On the evidence, it is difficult to place this eruption definitely in the group of profuse lentiginosis. It could possibly have been an example of telangiectasia macularis eruptiva perstans of Parkes Weber. Lack of histological examination makes the case of Finnerud (1927) impossible to classify.

The occurrence together of pigmented and vascular naevi was reported by Hermans and Schokking (1941), a report erroneously attributed to van Bruggen by Degos and Carteaud. These lesions were present at birth and had persisted in this man up to the age of 23. They were described as numerous small and larger brown and pinkish spots on the skin and mucous membranes, and intestinal bleeding was mentioned. Siemens commented on this case that it was an unusual freckle naevus combined with a naevus flammeus. The details given are very sparse, but it was obviously not an eruptive phenomenon. The case described by Kiess (1927) is likewise one of profuse pigmented naevi in an infant.

The most remarkable example of eruptive cellular naevi is the case described by Degos and Carteaud (1956) as *lentiginose profuse kératosique*. At the age of 19, a girl developed a large number of pigmented macules on both buttocks. Eighteen months later, spots came out in an explosive eruption and spread widely over the body and limbs. There was no preceding illness of any sort. The individual lesions were dark brown or black. Some were raised and had a detachable scale. When removed, the scale showed an area of pigmentation on the under surface which, the authors said, made it resemble black confetti. The skin between the spots was scaly, like ichthyosis. The authors specifically stated that there were no associated angiomas either clinically or histologically, rebutting a suggestion of Touraine that this condition might be related to diffuse angiokeratoma of Fabry. General examination showed no abnormality. The histological picture described was that of a naevoid lesion of the lentigo type, with hyperkeratosis and parakeratosis.

The case which I am about to describe had in common with those mentioned above the eruptive onset and symmetrical distribution. It differed in that the initial lesion was telangiectatic and only after several weeks did it develop the clinical aspect of a cellular naevus. I believe this case is in the same class as those of Darier, Balzer *et al.*, and Degos and Carteaud. With some diffidence I suggest that Darier's title should be altered to emphasize the eruptive rather than the profuse character of the affection. "Eruptive telangiectatic cellular naevi" would describe my case, "eruptive keratotic cellular naevi" that of Degos and Carteaud, and "eruptive cellular naevi" (or "lentiginosis") such cases as those of Darier and of Balzer *et al.*

CASE REPORT.

A man, aged 19 years, had a transient loss of consciousness in March 1958. He was referred to Dr. J. V. Gordon for neurological investigation. Whilst in hospital, he suddenly developed a rash on the trunk and proximal parts of the limbs. There was independent testimony from the nursing staff that the rash had appeared overnight and that new spots were still appearing. He had always had a few pigmented moles on the face and trunk. I was asked to see him a fortnight after the beginning of the eruption. He showed multiple telangiectatic blotches, mostly elliptical in shape and about 1.0 by 0.5 cm. in size, which were distributed symmetrically over the trunk and roots of the limbs, numbering about fifty or sixty in all. There were none on the face, hands or feet. Some were just palpably thickened and others were entirely

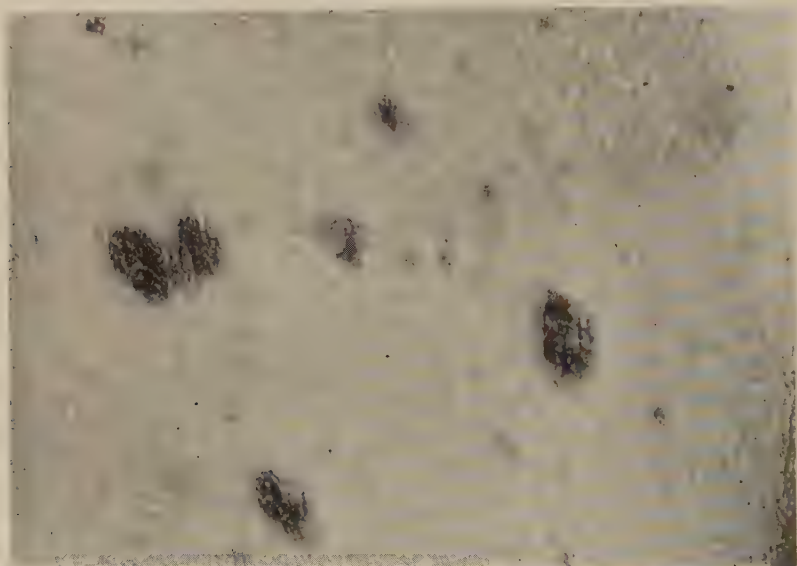


FIG. 1.—A group of eruptive cellular naevi on the posterior aspect of the right shoulder. The darker lesion on the left is a brown pigmented mole of some years' duration and the central blotch is an ephelis. The other four naevi had appeared during the previous three weeks. The uppermost one is noticeably less raised.

macular. The latter were mainly those which had appeared in the previous few days. Diascopy expressed all the colour from the macular lesions, but left a yellowish-brown stain in those on the trunk which were a week or two old. There was a marked contrast between the recent lesions and the dark brown of the moles that had been present for some years. During the next few days, I was able to observe some new lesions develop and at the beginning they were completely macular and angiomatic, arising from skin which had not previously shown any abnormality. During these few days, the older lesions became a darker brown colour and more raised, but did not extend peripherally. One such lesion was excised for microscopic examination about three weeks after the onset and the photograph shown in Fig. 1 was taken at the same time. General examination and neurological investigations revealed no abnormality and the cause of the loss of consciousness remained unexplained.

The biopsy specimen was embedded in paraffin and sections were stained with haematoxylin and eosin. These showed the features of an active compound cellular naevus. There was a moderate degree of acanthosis of the epidermis and an extreme

degree of proliferation of melanocytes at the epidermo-dermal junction which completely obscured the basal layer in places. Beneath this were groups of naevus cells, many of which were multinucleate. Superficially these cells were arranged in a disorderly fashion, but deeper in the dermis they formed a broad band and the individual cells were rather more regular. Coursing through this band of cells were numerous fine channels. In some of these, an endothelial lining could be seen. Some contained

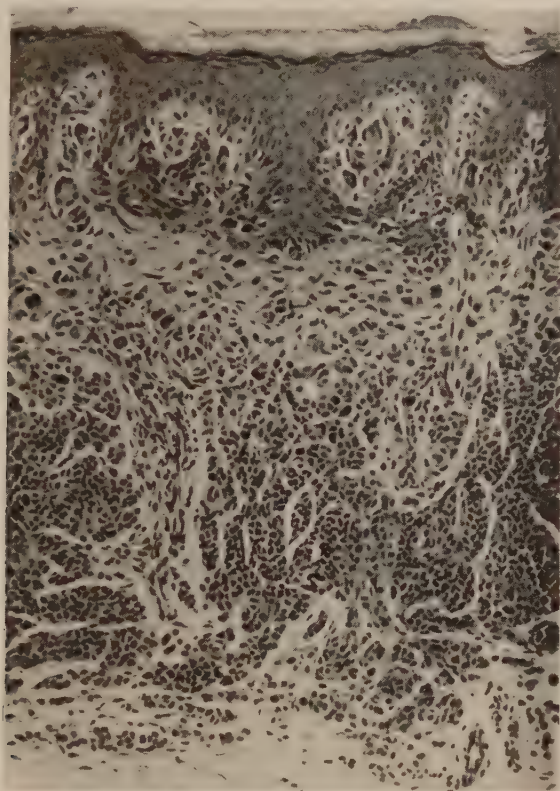


FIG. 2.—The section shows multinucleate cells among the proliferating melanocytes. The naevus cells are smaller and more orderly in the deeper parts. There are also many small blood vessels. Some of the clefts between the naevus cells are artefacts produced by shrinkage during fixation.

erythrocytes and anastomoses between neighbouring channels and to vessels of the subjacent plexus could be found. This was the histological counterpart of the clinical telangiectasia. They were relatively narrow capillaries whose course was mainly perpendicular to the skin surface. The naevus cells grew down into close relationship with these vessels and did not extend deeper than them. Evidence of melanin production was found in the form of melanin-laden histiocytes, both immediately beneath the epidermis and also among the deeper band of naevus cells.

DISCUSSION.

Pigmented naevi often darken and may increase in size at adolescence, during pregnancy or in the course of Addison's disease. These effects may

result from endocrine changes which release increased quantities of melanocyte stimulating hormone into the circulation. The type of case discussed here is different, in that a widespread and symmetrical eruption of cellular naevi occurs on skin which previously looked normal. The character of the eruption leaves no doubt that it is a response to a central stimulus but the nature of this stimulus is not known. In the case reported here, there was no change in the pigmentation of the normal skin or of pre-existent moles, such as might be produced by melanocyte stimulating hormone. Whether the disturbance of the central nervous system was related to the eruption is a matter for speculation.

The natural history of cellular naevi has been described in detail, but their cause remains obscure and they are usually considered to be developmental anomalies. There is reason for regarding them as due to more than localized hyperplasia of melanocytes, for other elements of the skin may show changes in the lesion. A common example is the coarsely hairy naevus in a finely hairy area. An excessive number of nerves or vessels may at times be found in sections of naevi, and ectopic fat cells are not infrequently seen between clusters of naevus cells in the upper dermis. It seems likely that there is an abnormality of the whole thickness of the skin in which the proliferating melanocytes and the naevus cells form the commonest and most conspicuous features.

The importance of the uncommon condition which forms the subject of this paper, therefore, is that it may throw some light on the stimulus which provokes cellular naevi to develop. It is possible that less dramatic examples of eruptive cellular naevi are not uncommon. Several unreported cases were mentioned when this subject was discussed at a recent meeting of the St. John's Hospital Dermatological Society.

SUMMARY.

A case is described of a man aged 19 years who developed a sudden symmetrical eruption on the trunk and limbs. The individual lesions were initially small telangiectatic macules, which became cellular naevi over the course of several weeks.

Microscopical examination of a developing lesion showed an active compound naevus with many capillary vessels running through the intradermal band of naevus cells.

Some previously reported cases of eruptive cellular naevi are discussed. It is suggested that the abrupt onset is of more significance than the profuse distribution, and that the term eruptive cellular naevi (or lentiginosis) is more appropriate than *lentiginose profuse* of Darier.

I am indebted to Dr. G. F. Donald, of Adelaide for taking the clinical photograph and to Mr. R. J. Lunnnon, F.R.P.S., Institute of Dermatology, for preparing the photomicrograph.

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NAEVOXANTHOENDOTHELIOMA WITH PIGMENTARY ABNORMALITIES.

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MCDONAGH (1912) reported five patients with lesions which he termed "naevi of the type of endothelioma". He suggested that as a result of a fatty change in the cells during their dissolution, a xanthoma-like condition was produced which he named naevoxanthoendothelioma. A few years earlier, Adamson (1905) had described essentially the same condition under the title "congenital xanthoma multiplex". Since these original descriptions, many further examples have been reported (Senear and Caro, 1936; Allington, 1937; Oliver, 1939; Zeisler, 1939; Rattner, 1948; Laymon and Schoch, 1949; Blank *et al.*, 1949; Nomland, 1954 and Helwig and Hackney, 1954).

Thannhauser (1950) regarded the condition as the monosymptomatic form of eosinophilic xanthomatous granuloma, related to the Hand-Schüller-Christian syndrome. The occurrence of lung lesions (Lamb and Lain, 1937), hepatosplenomegaly (Gans, 1959) and ocular involvement (Blank *et al.*, 1949; Gharib *et al.*, 1959) lends support to this view.

The eruption during infancy of scattered yellowish-orange nodules gives rise to the striking clinical picture, while the aggregation in the dermis of large cells with foamy cytoplasm and vesicular nuclei produces a characteristic histological appearance. Although Degos (1953) stated that individual lesions might become pigmented, an association of naevoxanthoendothelioma with other pigmentary abnormalities has not previously been stressed and may perhaps have been overlooked. The purpose of this communication is to report three patients with naevoxanthoendothelioma in whom such pigmentary abnormalities were present.

CASE REPORTS.

Case 1.—A boy first seen at the age of 1 year. When he was 8 months old, typical yellowish-brown naevoxanthoendotheliomatous nodules varying in size from 2 to 8 mm. appeared on the face, scalp and trunk. Two months later a few small brown macules were noticed on the trunk. When seen again at the age of 6 years, many of the previous naevoxanthoendotheliomatous lesions had disappeared, some leaving thin white depressed scars. Numerous brown macules resembling *café au lait* spots, were present on the trunk, neck and limbs. These were mainly round or oval and varied in diameter from 3 to 25 mm. The larger patches occurred chiefly on the chest, abdomen and legs while the smaller ones were aggregated around the neck and upper chest. No other abnormality was detected. There was no family history of xanthoma or neurofibromatosis.

Investigations.—Plasma cholesterol normal. Skiagrams of the chest and skeleton normal. Histological examination of a nodule from the scalp showed an infiltrate in the dermis consisting of uniform large pale cells with foamy cytoplasm and round vesicular nuclei (xanthoma cells) and a number of Touton giant cells. The overlying epidermis was slightly atrophic. A pigmented patch from the back showed an epidermis with a loose horny layer, conspicuous clear cells and an increase of pigment within the basal-cell layer. In the cutis a mild perivascular round-cell infiltrate was present.

Case 2.—A boy first seen at the age of 10 months with yellowish-orange naevoxanthoendotheliomatous nodules on the scalp which had appeared two months previously. An area of brown pigmentation in the region of the right shoulder had been present since birth. This consisted of a large central patch which was mildly hypertrichotic, surrounded by many irregularly shaped brown macules. Similar oval macules of varied size were present on the trunk and back. During the next eighteen months, several of the original naevoxanthoendotheliomata disappeared leaving only slightly wrinkled scars, but new lesions continued to appear on the face and trunk. The pigmented patches over the shoulder remained unchanged, but further pigmented macules varying from 3 to 20 mm. in diameter and resembling *café au lait* spots appeared on the trunk.

Except for a squint, there was no other abnormality. There was no history of skin disease or neurofibromatosis in the family.

Investigations.—Haemoglobin 92%. White cell count 8300 per cu.mm., mild eosinophilia. Platelets normal. Plasma cholesterol 237 mg./100 ml. Total serum protein 5.9 g./100 ml. The electrophoretic pattern was considered normal for a child of this age. Skiagrams of the chest, long bones and skull showed no abnormality. Histological examination of a nodule from the back showed the mid-corium to be occupied by masses of xanthoma cells separated by connective tissue. The overlying epidermis was normal. A pigmented patch showed an increase in the horny layer, marked hyperpigmentation and clear cells within the basal layer. A perivascular infiltrate was present in the dermis.

Case 3.—A girl first seen at the age of 9 months with a number of yellow dermal nodules varying in size from 2 to 8 mm. on the scalp, chest, groins, back and buttocks. These nodules, which showed the typical clinical features of naevoxanthoendothelioma, first appeared at the age of 3 months and were still erupting. In addition, a Mongolian spot approximately 5 cm. in diameter was present over the posterior aspect of the left shoulder (Fig. 1). No other pigmentary abnormalities were found. The edge of the liver was palpable but otherwise general examination was negative. There was no history of skin disease in the family.

Investigations.—Haemoglobin 84%. White cell count 9800 per cu.mm., normal differential. Plasma cholesterol 200 mg./100 ml. Serum proteins 6.4 g./100 ml. The electrophoretic pattern was normal. Histological examination of a nodule and the Mongolian spot showed the typical appearances of these two conditions.

DISCUSSION.

Naevoxanthoendothelioma is an uncommon condition and during the past seven years we have had only four cases, but in three of these, naevoid pigmentary abnormalities were present. Two had brown lesions of the *café au lait* type, while the third, a white child aged 9 months, had a large Mongolian spot.

The presence of pigmentary abnormalities in naevoxanthoendothelioma might be due to chance, but the association in three out of four cases suggests that this is unlikely. To determine the approximate incidence of such pigmentary abnormalities in children of the same age group, we have examined consecu-

tively 50 white children attending the skin department of a children's hospital. None of these children showed such pigmentary changes although two had hairy pigmented naevi.

Nomland (1954), reporting three cases of naevoxanthoendothelioma, includes the description and photograph of a 13 months old baby with typical *café au lait* lesions on the trunk. The distribution of these patches resembles that in



FIG. 1.

our Cases 1 and 2. Whittle (1958) presented a case of naevoxanthoendothelioma associated with multiple pigmented *café au lait* macules and Kinmont (1959) has a child under his care with naevoxanthoendothelioma, aortic stenosis and pigmented macules.

We feel that pigmentary abnormalities may not be uncommon in naevoxanthoendothelioma and that with increased awareness of this association more cases of it will be recognized. Such a combination may have an aetiological relationship and our findings lend some support to McDonagh's original view that naevoxanthoendothelioma is essentially a naevoid condition. The course and progress of the pigmentary anomalies is not yet known, but lesions are still appearing in our cases and so far none has disappeared. The clinical and histological features were quite unlike those of urticaria pigmentosa and no urtication occurred after friction or pressure. The pigmented patches resembled

closely the *café au lait* spots seen in von Recklinghausen's disease and may perhaps represent a *forme fruste* of that condition, although no other evidence of it was found in these children.

SUMMARY.

Three cases of naevoxanthoendothelioma with pigmentary abnormalities are reported. In two cases, pigmented patches resembling *café au lait* macules were present but no other evidence of neurofibromatosis was found. The third case showed a Mongolian spot. Evidence of this association has been found in the literature. The high incidence of such pigmentary abnormalities in children with naevoxanthoendothelioma compared with others of similar age suggests that the association is more than fortuitous. The few previous case reports have not stressed the significant association of these two conditions. It seems likely that further cases will be found if they are sought.

We are grateful to Dr. D. I. Williams for permission to include Case 1 in this report. We wish to thank Dr. M. E. A. Powell for help with the histology and Mr. W. Smith for the photograph.

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HEREDITARY HÆMORRHAGIC TELANGIECTASIA

A STUDY OF A FAMILY WITH SIX CHILDREN

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THE first description of hereditary haemorrhagic telangiectasia was given by Babington (1865). He recorded epistaxis in five generations of a family but gave no account of the lesions. Legg (1876) however drew attention in his cases to naevi on the face, forehead and trunk. He felt that the disease was a form of haemophilia due to congenital vascular weakness. Chiari (1887) diagnosed haemophilia in his cases and suggested that the lesions were caused by rather than the cause of the bleeding. Chauffard (1896) also felt that the lesions were stigmata of an atypical form of haemophilia though he did recognize that bleeding took place from them. Rendu (1896) was the first writer who had a proper understanding of the disease. He pointed out that the tendency to bleed in the case of injury not involving the lesions, such as dental extraction, was not greater than in normal people and he therefore felt that the condition was a form of pseudohaemophilia. He described the lesions of the skin and mucous membrane and observed that the skin lesions could be made to blanch by pressure but always returned. Further descriptions were given by Osler (1901) and Parkes Weber (1907) and the condition is sometimes referred to as "Rendu-Osler-Weber disease". The name hereditary haemorrhagic telangiectasia is due to Hanes (1909). Parkes Weber recorded that both sexes were affected by the disease and could transmit it. In his cases, lesions were not recorded until middle age though the tendency to epistaxis may have been present from an early age. Garland and Anning (1950) in their description of twenty families observed a few lesions in infancy but in most affected individuals they did not become conspicuous until after puberty.

The diagnosis of hereditary haemorrhagic telangiectasia in a girl with five young siblings provided an opportunity to undertake a family study with particular reference to the incidence of the disease in childhood. Two members of the family suffered from fits and the possibility that this is related to the disease is considered. The family tree is shown in Fig. 1.

CASE RECORDS.

A girl aged four and a half years was referred to the Hospital for Sick Children on account of a port wine stain of the face (Fig. 2). The lesion had been noted at the age of one and had gradually increased in size, bleeding once when injured. A smaller lesion had been noted on the back of the right hand one year previously.

There was no history of fits or epistaxis. On examination there was a raised area of variable erythema measuring half an inch by two and a half inches, situated below the right zygoma. Pressure at several points caused the almost complete disappearance of the erythema. There was a typical spider lesion on the dorsum of the right hand and there were two pinpoint lesions, one on each ear. There was no involvement of the mucous membranes nor was there any definite evidence of adenoma sebaceum. These findings in conjunction with the family history of epistaxis led to the diagnosis of hereditary haemorrhagic telangiectasia being made. The facial lesions were successfully treated by electrocoagulation.

Investigations.—Skiagram of chest normal. Hb. 12.6 g. %. M.C.H.C. 32%. W.B.C. 10,600 per cu. mm. with normal differential. Platelets normal. Bleeding time (Duke) 6 minutes. Clotting time (Dale and Laidlaw) 2 minutes 10 seconds. E.E.G. showed a moderate but definite abnormality, more marked over the right than over the left hemisphere. There were no focal signs.

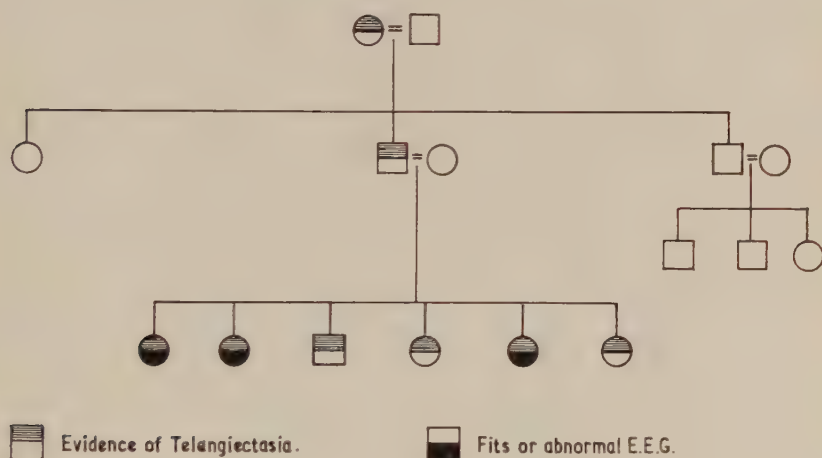


FIG. 1.

(This case was shown by Bloom at a meeting of the Section of Dermatology of the Royal Society of Medicine on 19 November 1959.)

Family history.—Paternal grandmother, aged 84. She could not recall evidence of the disease in her late husband nor in any of their parents but had noted involvement of her own face in the previous four years. On examination there were several nodular lesions of the face which blanched on pressure but the mucosae were healthy. There had been no convulsions or epistaxis.

Father, aged 46. He is said to have had lesions on his neck at birth which gradually spread over his face. At the age of twelve years, the facial lesions were treated with carbon dioxide snow. He has suffered from mild epistaxis since the age of sixteen but has had no other complications of the disease. On examination his colour was good and there was widespread involvement of the face with pinpoint and nodular lesions. Typical lesions of the nasal mucosa were seen. E.E.G. was normal. He is not related to his wife who showed no evidence of the disease.

Paternal uncle and aunt. Showed no definite evidence of the disease. Examination of the three children of the uncle, who were said to be unaffected, was not permitted.

Sister, aged 15. She has suffered from epistaxis since the age of nine to ten years. Facial lesions were first noted when she was thirteen. During a six-month period

at the age of three, she had fits when she went red in the face, lost consciousness, clenched her fists and fell over. On examination, her colour was good and there were multiple pinpoint lesions of the face and typical lesions of the nasal mucous membranes. E.E.G. showed a mild but definite abnormality about the right temporal and temporo-occipital region, suggesting the possibility of a discrete discharging area.

Sister, aged 12 (Fig. 3). She has suffered from epistaxis since the age of seven years. The same year she began to suffer from fits of which she has had as many



FIG. 2

as fifteen a day lasting a few seconds only. She would develop a glazed look and lose consciousness, falling and hurting herself badly on several occasions. The arms went stiff and there was jerking of the legs. She was sometimes incontinent of urine. Occasionally there was warning of these episodes. In September 1955, she was referred to the out patients department of another hospital where she was started on tridione 0.3 g. thrice daily. E.E.G. at this time was normal. In January 1956, benzedrine was added to this therapy and she improved. However in May 1957, the fits returned and she was admitted to the same hospital. Several attacks occurred whilst under observation. There was no loss of consciousness during these episodes. E.E.G. showed a preponderance of activity in the left temporal zone and the pos-

sibility of temporal lobe epilepsy was considered. However the behaviour of the child had suggested that psychological factors might be important and it was wondered whether she might improve as an out patient without drug treatment. The fits increased in frequency and six weeks later benzedrine and tridione were restarted. In October 1957, E.E.G. suggested the possibility of an expanding lesion in the left frontal region. At this time she began to be increasingly troubled by attacks at night and in February 1958, phenobarbitone "Spanule" 1 grain nightly was added to the therapy with good results. In March 1959, she was given mysoline 250 mg. twice daily and the other treatment was stopped. She has had six attacks in the last



FIG. 3.

ten months. E.E.G. in April 1959 revealed a maximal disturbance in the left temporal lobe and in December 1959 a moderate diffuse abnormality without constant focal features. Facial lesions have been present since the age of about nine years, and these had, at different times, raised suspicions of acne and tuberosc sclerosis. On examination, her colour was good and there were numerous pinpoint lesions of the face and several large lesions of the nasal mucosa. There were no neurological signs. She was mentally retarded, but there was no definite evidence of adenoma sebaceum.

Brother, aged 8. He has suffered from epistaxis since the age of six years but there have been no fits. On examination his colour was good and there were early lesions of the nasal mucosa and one pin-point lesion of the face.

Sister, aged 6. There was no history of fits or epistaxis. On examination the mucosae were healthy but three spider type lesions were found over the upper limbs.

Sister, aged 2. There was no history of fits or epistaxis. On examination the mucosae were healthy but two pinpoint lesions were found on the face.

DISCUSSION.

Steiner (1917) described three types of lesion in this disease, the pinpoint, spider and nodular. Typical pinpoint lesions are best seen on the face as in this family, the spider type over the limbs and the nodular type on the mucous membrane—but all of these lesions can be found in any situation. In the case of the four and a half year old child, an aggregation of facial lesions produced an appearance not unlike a port wine stain but distinguished from it by being raised and capable of obliteration by pressure.

Lesions are now known to occur in all organs of the body and haemoptysis, gastro-intestinal bleeding, haematuria and intracranial haemorrhage have been recorded though in all descriptions, epistaxis is the most common complication. Hodgson *et al.* (1959) described the less common complications in their study of 231 of 330 descendants of a sufferer from the disease. Thirty-nine per cent of those seen were affected and of these fifteen per cent were found to have pulmonary arteriovenous fistulae.

Two members of the family we have seen have suffered from fits and these and one other have abnormal electro-encephalograms. It is tempting to speculate that these are manifestations of the disease. In the case of the thirteen-year-old girl, the character of the fits has changed and the electro-encephalogram has been very variable. Courville (1957) described clusters of enlarged and tortuous veins of the brain and meninges in this condition and it may be that haemorrhages from this abnormal vasculature are responsible for the neurological disturbance. Campbell (1944) suggested that intracerebral telangiectasis might have caused migraine in one of his patients with the disease. Hodgson *et al.* (1959), however, found only three of 231 sufferers of the disease who had fits. Four others had episodes of weakness and paresthesiae and three had had premature cerebrovascular incidents. Boder and Sedgwick (1958) drew attention to the relationship between telangiectasia of the bulbar conjunctiva, cerebellum and cerebellar meninges and ataxia, and further cases have been described by Siekert *et al.* (1959).

SUMMARY.

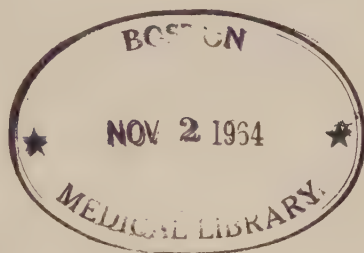
A family suffering from hereditary haemorrhagic telangiectasia is described. Evidence of the disease was found in all six children aged two to fifteen years. Of the eight affected members, four suffered from mild epistaxis. The lesions were predominantly facial and in one case superficially resembled a port wine stain.

Two members of the family suffered from fits and another had an abnormal electroencephalogram. The possibility is considered that fits due to haemorrhage from abnormal intracranial vessels might be a feature of the disease.

We wish to thank Mr. Derek Martin who prepared the illustrations.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Professor J. T. INGRAM.

MEETING HELD AT THE LONDON HOSPITAL.

18 June 1959.

Ectodermal Defect (Epidermolysis without Bulla Formation).—Dr. J. S. PEGUM.

A boy aged 4 years.

Since he started to crawl, wherever he has injured the skin it has "come off". Has poor teeth. Father and mother are cousins. Other members of the family have had defects of the skin and teeth.

Examination.—Dry, scaly skin on the arms, legs and face. Angular stomatitis and crusting of nostrils. Punctate keratoses on knees and elbows. On hands and knees especially where the skin has been knocked, the upper layers of the skin appear to have come off. Teeth: hypoplasia and caries.

Bullous Pemphigoid, Hypertension, Psoriasis.—Dr. BRIAN RUSSELL.

A woman aged 57.

History.—Nine years ago, onset of nummular psoriasis involving trunk and limbs. Five years ago, developed blisters in the mouth followed by a bullous eruption in the right groin. She was admitted to hospital and treated with cortisone. During the following seven months sudden relapses as an out-patient necessitated two further admissions. Her blood pressure during this time varied between 180/120 and 195/130 mm. Hg. On her second admission there were superficial ulcers with erythema and oedema in the axillae and groins and on the arms and tongue. She responded well to cortisone and corticotrophin. She relapsed shortly after discharge. Though the dose of cortisone was increased the pemphigus did not improve and the psoriasis grew worse. Following discharge after her third admission she continued to get oral and flexural lesions. The cortisone was increased to 150 mg. daily.

Four years ago her blood pressure rose to 214/130 mm. Hg. Cortisone 100 mg. daily was required for adequate suppression of the eruption. Three years ago, complained of headache. Blood pressure 240/140 to 300/180 mm. Hg. No cardiovascular changes were found. Two and a half years ago, cortisone withdrawn and prednisone 15 mg. daily substituted. One year ago, hypertensive retinopathy developed. Blood pressure 240/150 mm. Hg. Treated with reserpine and mecamlamine. There has been little change since then. The blood pressure varies from 220/130 to 270/145 and headaches are still severe. Dosage of prednisone below 10 mg. daily results in reappearance of lesions.

Examination.—Residual scarring of flexural and oral ulceration. Nummular psoriasis of trunk and limbs.

Histology.—Vesicles apparently related to tangentially cut rete pegs containing numerous eosinophils. Heavy infiltration by eosinophils in dermis. Vesicular dermatitis consistent with bullous pemphigoid.

Comment.—Bullous pemphigoid and psoriasis running independent courses. Hypertension increased during steroid therapy. The bullous eruption has been well

controlled by prednisone, the psoriasis being unaffected. Both the bullous eruption and the psoriasis are well controlled by triamcinolone.

THE PRESIDENT: I am interested to see the combination of psoriasis and bullous or pustular eruptions.

Dr. LOUIS FORMAN: I have had a patient treated with quite reasonable doses of steroids whom we knew had benign hypertension; that patient, a woman, was treated for scleroderma and went quite suddenly into malignant hypertension and died. I do not think there is any doubt that if the patient has hypertension one must expect to run into trouble on that score.

Sarcoid Following Wounds: Syphilis.—Dr. PETER SMITH.

A builder's clerk aged 41.

History.—1942, Egypt, flesh wounds back and right elbow; bilateral below knee amputations. Metallic fragments were extruded from the back and elbow over the next fifteen years. 1956–7, nodules appeared on the wound scars. 1957, similar nodules came on right side of nose and cheek.

Clinically and histologically the diagnosis was made of lupus vulgaris following trauma and the elbow and back nodules disappeared after isoniazid had been taken for six months. The face nodules improved at first, but under continued treatment have increased in number.

Examination.—April 1959. Right elbow, left back and buttock, scars without infiltration or erythema. Translucent reddish nodules 5–7 mm. diameter over nose, upper lip and right naso-labial fold.

Investigations.—Biopsies: Elbow and back, 1957, face, 1959. Heavy infiltration of epithelioid cells and lymphocytes. Occasional giant cells and some areas of eosinophilic necrosis. No A.F.B.

Silica was injected intercutaneously and a nodule was excised a month later: this showed a collection of histiocytes containing granules which were not doubly refractile. No inflammatory infiltrate.

Skiagrams: Chest, 1959, no active lung disease. Lumbar region, 1957, metallic foreign bodies in back and left chest wall.

Tuberculin test: 1 in 10,000—positive.

W.B.C.: 8300, normal differential.

Serum proteins: Albumin 4.5 g. Globulin 2.2 g.

E.S.R. 1959: 24 mm. in one hour.

A Wassermann reaction was positive, as was the trepomena immobilization test.

Dr. H. HABER: Tuberculoid structures always call for a Wassermann test.

Dr. BRIAN RUSSELL: I suggest that this is sarcoidosis in a man with a positive Wassermann reaction; the physical signs suggest sarcoidosis rather than syphilis.

Urticaria Pigmentosa.—Dr. J. S. PEGUM.

A housewife aged 46.

History.—Twenty years ago, onset of pigmented papular rash which slowly spread over arms, legs and trunk. Irritation and urtication of lesions is produced by heat, worry and eating cheese or fish. Aspirin has no effect. Eighteen years ago, the rash cleared at the sixth month of pregnancy, but returned soon after delivery.

Two years ago, treated with prednisone 20 mg. daily for 1 year without effect.

Examination.—Widespread pigmented papular rash on arms, legs and trunk. The rash on the abdomen is localized especially to the striae atrophicae.

Investigations.—Blood count and bone and chest skiagrams normal. Skin biopsy showed moderate upper dermal infiltration by mast cells with cytoplasmic granules showing metachromasia—urticaria pigmentosa.

Comment.—A case of urticaria pigmentosa which cleared during pregnancy but which was uninfluenced by steroids.

THE PRESIDENT: The history in relation to pregnancy is interesting. In Vienna we saw a woman patient aged 80 with similar extensive lesions. There was the same involvement of striae over the abdomen. In Vienna they are treating urticaria pigmentosa with injections, three or four times a day over a fortnight, of a mixture of Largactil and phenergan which is said to reduce mast cells experimentally in animals.

Cutaneous Granular Cell Myoblastoma.—Dr. C. M. RIDLEY.

A housewife aged 49.

History.—For 9 months, a lump on left flank.

Examination.—Yellow firm, smooth, cutaneous plaque, 1 cm. by 2, lichen planus elsewhere.

Histology.—Granular cell myoblastoma—cords and masses of pale staining, sometimes syncytial cells, containing many granules. No pseudoeitheliomatous hyperplasia.

Pigmentation from Prolonged Application of Mercurial Ointment.—Dr. BRIAN RUSSELL.

A man aged 51, a cashier.

History.—Daily application of Golden Eye Ointment to skin around the eyes for twenty-five years.

Examination.—Peri-orbital slate coloured pigmentation.

Dr. T. B. FITZPATRICK: The pigmentation is directly related to the presence of mercury in the dermis: the metal occurs in the form of coarse granules contained in histiocytes.

Dr. G. C. WELLS: A similar case of hydrargyria was shown at a meeting of this section in December 1955 (Cardnoe and Meara, 1956). Dr. Meara took a biopsy from the eyelid and we showed the pigment to be present as tiny refractile granules within the macrophages in the upper corium. The metal could easily be removed with iodine but we do not know exactly in what form the mercury is deposited.

Dr. H. HABER: Metal particles such as mercury or silver are easily made visible by dark ground illumination.

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The following cases were published in *Proc. R. Soc. Med.*, **52**, 1033.

Two Cases of Haemangioma Showing Delayed Natural Resolution.—
BRIAN RUSSELL, M.D., F.R.C.P.

Erythrodermia. Idiopathic Steatorrhoea.—BRIAN RUSSELL, M.D., F.R.C.P.
Lupus Erythematosus. Polymyositis.—WALLACE WHITE, M.B.

The following cases also were shown:

Ehlers-Danlos Syndrome.—Dr. C. M. RIDLEY.

Acanthosis Nigricans, Juvenile Type.—Dr. BRIAN RUSSELL.

Chronic Erythema Multiforme.—Dr. C. M. RIDLEY.

Pemphigus Foliaceus.—Dr. J. S. PEGUM.

Pemphigus Vulgaris; Osteomyelitis of Hand, following Steroid Therapy.
—Dr. BRIAN RUSSELL.

Pemphigus Vulgaris.—Dr. C. M. RIDLEY.

Hansen's Disease. Foot-drop. Tendon Transplant.—Dr. BRIAN RUSSELL.

Sarcoidosis: Lupus Pernio.—Dr. J. S. PEGUM.

Psoriasis showing Remission following Psychotherapy.—Dr. JOHN COWIE.

Pigmentation Due to Red Rubber Colostomy Belt.—Dr. J. S. PEGUM.

Atrophie Blanche.—Dr. BRIAN RUSSELL.

Atrophic Lichen Planus.—Dr. WALLACE WHITE.

Dermatomyositis.—Dr. J. S. PEGUM.

Basal Cell Carcinoma Treated by Dermabrasion.—Dr. C. M. RIDLEY.

Xanthomatosis; Xanthoma Tendinosum.—Dr. N. A. THORNE.

Benign Familial Pemphigus.—Dr. BRIAN RUSSELL.

President—Dr. HUGH GORDON.

15 October 1959.

Cutaneous Metastases.—Dr. H. T. H. WILSON.

A. R.—, male, aged 36. Butcher.

History.—In March 1959 he suffered an acute febrile illness, with right-sided pleurisy and cough with mucoid sputum. His cough has persisted since.

Early in August 1959, while in Spain he developed a nodule on his shin, which subsequently ulcerated. Later he developed similar lesions in the right forearm, the left fibula and on the scalp.

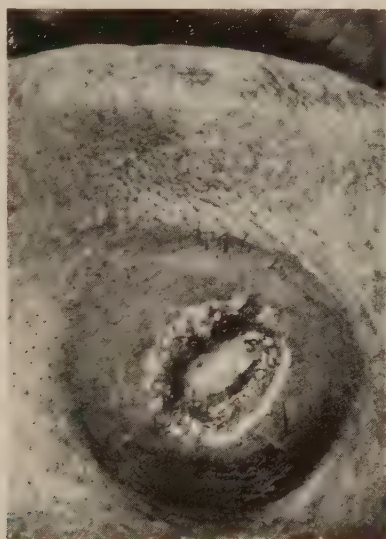


FIG. 1.

On examination.—He has a nodule on the chin about 2 cm. diameter, with a necrotic purulent centre (Fig. 1). There is a similar lesion on the vertex of the scalp.

Investigations.—*Chest X-ray:* There is a mass in the right upper lung field posteriorly, the remainder of the lung fields are clear and the heart normal. No evidence of mediastinal glandular enlargement.

? Carcinoma of the posterior apical position of the right upper lobe.

Biopsy: Differentiated squamous cell carcinoma. There is no clear indication from the section as to whether this lesion is primary or metastatic.

W. R.: negative. *Meinicke reaction:* negative. *Swab:* Culture—*Staphylococcus aureus*.

Dr. C. D. CALNAN: May I ask for Dr. Haber's evidence for saying that the diagnosis in this case is other than as presented? Dr. H. HABER: The specimen shown to me exhibits pseudo-epitheliomatous downgrowth of the epidermis as seen in keratoacanthoma. This feature is definitely not in keeping with a secondary deposit.

The following cases have been published in *Proc. R. Soc. Med.*, **53**, 295.

Two Cases of Basal-Cell Congenital Naevus.—Mr. PATRICK CLARKSON, F.R.C.S. and Dr. HAROLD WILSON.

Pyoderma Gangrenosum.—Dr. D. S. NACHSHEN (for Dr. I. MUENDE).

The following cases were also shown :

Two Cases of Familial Rosacea-like Dermatositis with Lanugo Hair Changes.

—Dr. H. WILSON.

Lupus Vulgaris Treated with Diethyl Dithiolisophthalate.—Dr. C. W. MARSDEN.

Eczema Vaccinatum.—Dr. J. MORGAN.

Multiple Basal Cell Epitheliomata.—Dr. O. L. S. SCOTT and Dr. D. BETT.

Case for Diagnosis. ? Polyarteritis Nodosa.—Dr. E. N. M. JOHNSTON.

19 November 1959.

Pyodermia Chancriformis Faciei.—Dr. L. FORMAN.

A man aged 35. Dental surgeon.

Past history.—Three years ago, the patient was in hospital with rigors and fever of unknown origin. The blood count was normal.

Present disease.—Six separate necrotizing granulomata involving the eyelids have appeared over the past two years. Two of these lesions have been observed. The first seven months ago in the involuting dry crusted phase, having been present six

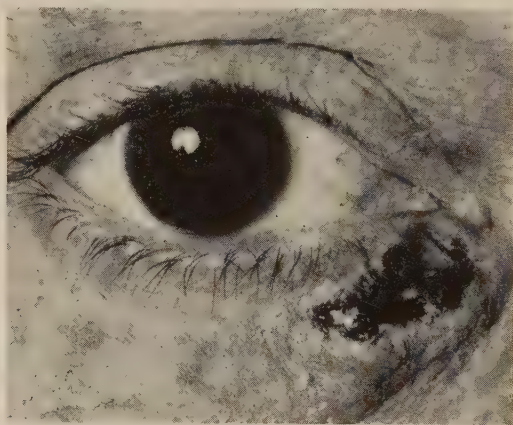


FIG. 1.

weeks and healing completely within a further two weeks (Fig. 1), to leave a superficial scar.

The present granulomatous nodule on the inner part of the upper eyelid has been present for four weeks (Fig. 2). It took three weeks to reach the present peak size and then became necrotic. It was originally a firm nodule 1 cm. across ; the surface became eroded and covered with a heavy yellow crust. Two small yellowish nodules in the immediate neighbourhood, the patient says, represent the early stages of the granuloma. There is some oedema of the eyelid, but no regional lymphatic enlargement or constitutional disturbance.

Investigations.—W.R. and Kahn negative. Culture from the ulcer *Staph. albus*. Total W.B.C. 11,600, polymorphs 70%, eosinophils 5%, lymphocytes 22%, monocytes 3%.

Treatment of the previous lesions with local and systemic antibiotics has been without influence on the course of the nodular or granulomatous crusted phase.

Comment.—Frain-Bell (1957) has described three cases of this condition and referred to Hoffmann's original paper. The face, particularly the eyelids, appears to be the site of election. The appearance and course of the granuloma are sufficiently characteristic to suggest that it is a clinical entity. I believe the two small nodules to be abortive phases of the granuloma. They disappeared without breaking down.

It has been suggested that it is a peculiar response to the *Staph. aureus*, the only organism recovered.

One of Frain-Bell's patients, a 61-year-old woman, presented a painless ulcer on the eyelid and three non-tender, firm brown nodules over the chest, one of which showed an early necrosis. The genesis of the disorder might be illuminated in the future by the histology of one of the early papules.

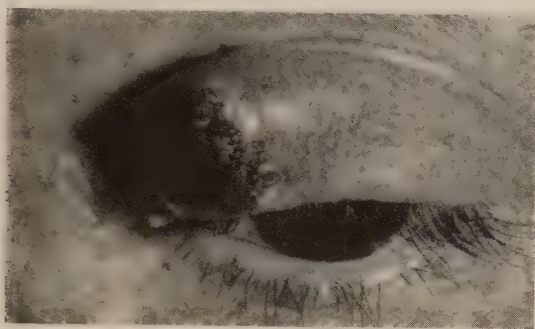


FIG. 2.

REFERENCE.

FRAIN-BELL, W. (1957) *Brit. J. Derm.*, **69**, 19.

Dr. G. A. GRANT PETERKIN : I presume Dr. Forman made a test for bromides?

Dr. G. B. DOWLING : Does Dr. Frain-Bell know what the long-term natural history of this condition is?

Dr. FRAIN-BELL : I have little to add to what Dr. Forman has already said. One of the three cases of pyoderma chancriformis faciei that I reported in 1957 (Case 1) has been seen by me on a number of occasions since then with recurrent lesions. As Hoffmann (1934) pointed out the face and the eyelids are the most commonly affected sites.

As to the long-term natural history of the condition, which Dr. Dowling asked about, this is well portrayed in the example which we saw today. The initial lesion is a small papulo-pustule, which may slowly grow or remain quiescent for a week or two and then ulcerate with rapid enlargement to form the classical hard chancriform button which Hoffmann described. There may be again a quiescent period, followed by a fairly rapid healing phase, the total duration of the lesion usually varying from four to eight weeks. I have been impressed by the complete freedom from pain of these destructive ulcers.

My views on the aetiology are the same as Dr. Forman's. I was not successful with the use both systemically and locally of the appropriate antibiotics in altering the natural history of the individual lesion except in so far as it may reduce the total duration.

REFERENCE.

HOFFMANN, E. (1934) *Arch. Derm. Syph., Berlin*, **170**, 403.

The PRESIDENT : For how many years had the female patient had the lesions?

Dr. FRAIN-BELL : I believe she has been developing these lesions for nearly five years.

Dr. I. B. SNEDDON : Has anyone investigated herpes antibody levels? The lesion seems to behave very like recurrent herpes simplex.

Dr. C. D. CALNAN : These lesions do not always run exactly the same clinical course. I saw a very typical example on the eyelid of a patient in Frankfurt a few years ago, which had resisted all treatment for many months. I do not feel that the evidence in favour of a staphylococcal pathogenesis is conclusive, although some cases repeatedly grow this organism.

Dr. L. FORMAN : There has not been a test for bromide. So far as I know a virus has not played any part at all.

Colloid Degeneration of the Skin Occurring in Brother and Sister.—Dr. R. V. HARRIS.

A girl aged 11 (S. T—).

A boy aged 10 (D. T—).

History.—Red patches on both cheeks were first noticed by their mother when they were about 9 months old. In both children these gradually extended down the cheeks and on to the chin and forehead. They were made worse by exposure to bright sun and cold winds. There has never been any general reaction to sunlight.

At the age of 5 they were seen by Dr. J. F. Wilkinson and at that stage there were sharply defined, symmetrical, reddish-brown areas with minimal scaling and a certain amount of induration, but there were no atrophic changes. The possibility of a peculiar form of light sensitivity was considered.

Since then numerous small pitted scars have developed on the cheeks, nose and forehead in both. These areas are liable to bleed after light trauma, i.e. rubbing with a face flannel or towel. S. T— picks at her face which results in bleeding and scarring.

General health has been good and development normal in both children. No skin lesions have been present on the hands or other parts of the body.

Family history.—Nil relevant.

Clinical findings.—S. T—. Symmetrical, reddish-brown, raised and slightly indurated areas on both cheeks (Fig. 1). Scattered over these areas on the nose and to a lesser extent on the forehead and chin, are numerous depressions varying in size and shape. Some are small, circular and pinhead in size, others are linear streaks, 10–15 mm. long. The skin on the outer regions of the cheeks is smooth, almost waxy in appearance. Just below the eyes the surface is rough with minute discrete pseudo-vesicles. On lightly traumatizing these areas, small haemorrhages occur in the skin. Other areas of the skin are normal.

D. T—. Symmetrical, well defined, erythematous areas on both cheeks and chin (Fig. 2). Slight induration in the upper parts of the cheeks. Multiple pits and shallow depressions, varying in size and shape, some of which are linear, on both cheeks and nose. Patches of pigmentation on the forehead and nose. Small purpuric lesions have been seen from time to time—the result of rubbing. Other areas of the skin are normal.

Investigations.—Blood counts normal.

Urinary and faecal porphyrins within normal limits.

Biopsy D. T— (1953).—"There is a localized area of thinning of the epidermis with marked homogenization of the immediate sub-epithelial collagen. At first sight, this strongly suggested amyloid but all attempts at histochemical identification failed. The material does not give the usual reactions for collagen, but may well be a degeneration product of it. Deep to this zone and scantily within it are numbers of chronic inflammatory cells. Vessels and fat appear normal." (Dr. Kurrein.)

Biopsy S. T— (1959).—"The papillary and subpapillary layer of the corium shows a sharply demarcated continuous band of homogenized collagen leading to atrophy of the overlying epidermis and intervening rete pegs. Numerous capillaries cross the degenerated area producing many clefts with the rigid tissue.

"Stains : *Congo red*—faintly metachromic; *Methyl violet*—negative; *Van Gieson*—pale pink in contrast to bright pink of normal collagen; *Reticulin*—negative; *P.A.S.*—negative.

"The changes somewhat resemble those found in colloid milium." (Dr. H. Haber.)



FIG. 1.



FIG. 2.

Comment.—These cases are shown because of the unusual age of onset and the fact that no similar clinical picture can be discovered in the literature.

Dr. J. F. WILKINSON : The appearance in March 1953 was different from today's in that there was sharper demarcation and a certain amount of induration. The areas affected were reddish-brown and the skin quite smooth, almost waxy. On exposure to sunlight or cold winds, there was fine scaling. I wondered whether these cases were going to develop into atrophoderma reticulata but the histology was against the diagnosis. There were no abnormal porphyrins in the urine or faeces. As I see the lesions today their margins are less demarcated and there is some atrophy. Pitting was not present when I saw the children originally although two or three pits appeared about 1955. There has been some improvement in the appearance of both children. I should like to know the prognosis.

Dr. H. HABER : The lesion shows quite characteristic features of colloid degeneration of the upper cutis. There are masses of homogenous amorphous material lying as a broad band under the epidermis, which is atrophic. There is no specific stain for colloid. Stain for amyloid was negative. Colloid is regarded as a degenerative product of collagen after it has passed through the stage of basophilic degeneration. Others subscribe to the view that colloid is a deposit from the blood stream.

Dr. G. A. BECK : It is interesting that Dr. Wilkinson thinks that their condition is better than it was. Their father will be particularly gratified, for he told me this afternoon that it was because they had been so impressed with the improvement after a holiday in Eastbourne that he asked for his own transfer to Eastbourne so that the children could live there. He says that after the first day in the sun there is more redness of the affected areas of skin, but that thereafter it seemed to him to improve the more they were in the sun.

Dr. K. V. SANDERSON : Colloid degeneration of the skin is not uncommon in Australia. I have seen several cases there, and in all of them the histopathological features were the same as those Dr. Haber has described in these two children. In Australia the lesions occur mostly on the face, particularly on the nose and malar eminences, and on the back of the hands; and the patients engage in work which causes them to be exposed to sunlight. One of my patients was a fair-skinned red-headed Irishman, and another was a swarthy Italian. The Irishman had very much more prominent lesions, although the period of his exposure to the sun in Australia was much less than the Italian's.

I was interested in Dr. Harris' description of bleeding of the lesions on slight trauma. Another patient of mine with this condition developed petechial bleeding in the skin over lesions of the back of the hand after any injury.

The following cases have been published in *Proc. R. Soc. Med.*, 53, 298.

Pemphigus Vegetans Complicated by Peripheral Vascular Disease.—Dr. MAURICE GARRETTs (for Dr. P. J. HARE).

Pemphigus Foliaceus Complicated by Peripheral Vascular Disease.—Dr. MAURICE GARRETTs (for Dr. P. J. HARE).

Hereditary Haemorrhagic Telangiectasia.—Dr. V. R. BLOOM (for Dr. E. J. MOYNAHAN).

Stasis Syndrome mimicking Kaposi's Disease.—Dr. P. J. HARE.

The following cases were also shown :

Kaposi's Sarcoma.—Dr. A. B. SHRANK (for Dr. F. RAY BETTLEY).

Chronic Moniliasis.—Dr. R. H. MEARA.

Lichen Nitidus.—Dr. R. H. MEARA.

Facial Lesion for Diagnosis.—Dr. P. J. HARE.

17 December 1959.

Thyrotoxicosis with Circumscribed Myxoedema and Exophthalmos.—Dr. M. A. SMITH (for Dr. P. F. BORRIE).

A man aged 24. Press operator.

History.—1955 : Thyrotoxicosis and exophthalmos for eight months followed by partial thyroidectomy. After the operation the exophthalmos increased and six months later sub-cutaneous nodules were noticed on the shins and then elsewhere.

The patient gained weight at this time. After this the exophthalmos remained unchanged until the last few months but the skin nodules slowly increased. 1958 : Seen in Out-patients, condition on examination was as now. 1958 (March) : Investigated as an in-patient. 1959 (August) : Tarsorrhaphies first performed.

Family history.—No thyroid trouble.

Clinical examination.—*Skin* : Soft, pale, discrete papules and nodules up to 2 cm. in diameter are present on forehead, cheeks, upper sternal zone, shoulders and back, especially down mid-line.



FIG. 1.

Folds of hypertrophic skin and myxoedematous tissue cover most of the shins, and some plaques extend posteriorly (Fig. 1).

There is thickening of scars on both forearms sustained at work eighteen months ago and of a scar on the dorsum of the right foot where a lymphangiogram was done two years ago. Thyroidectomy scar not affected.

Comedones and pustules are present on the back, many of the lesions being infiltrated by myxoedematous tissue. The uninvolved skin is normal in texture.

Other abnormalities.—Husky voice. Bilateral exophthalmos with tarsorrhaphies, clubbing, marked of fingers and slight of toes. Palpable right lobe of thyroid gland.

Investigations and treatment.—March 1958 : Protein bound iodine 7.2 $\mu\text{g.}\%$. Serum cholesterol 215 mg.%. B.M.R. plus 17%. E.C.G. normal. Radio-iodine uptake indicated slight hyperthyroidisms.

Following treatment with Carbimazole—15 mg. t.d.s. for six weeks as an in-patient the levels changed to protein bound iodine 4.2 $\mu\text{g.}\%$, serum cholesterol 328 mg.%. B.M.R. plus 2% 1-thyroxine 0.1 mg. b.d. was added and the patient discharged.

Other treatments tried during the ensuing months were : tri-iodothyromine 25 $\mu\text{g.}\%$ daily with Lugol's iodine for six weeks.

X-ray therapy to orbits and shins (500 r in daily doses of 50 r at 250 KV)—d-thyroxine from 1 to 2 mg. daily for four months.

None of these treatments had any sustained effect on the clinical condition. In September 1959 protein bound iodine was 9.4 $\mu\text{g.}\%$, serum cholesterol 150 mg.% and B.M.R. plus 34%.

Present treatment.—Carbimazole 5 mg. t.i.d.

Comment.—This patient is presented on account of the extent of the skin lesions and of the deposits in the scars, and the failure of a variety of treatments to influence the course of the condition significantly.

Dr. F. F. HELLIER : Was mucin found in the lesions on the forehead? I ask because the appearance here resembles that in a patient described by Degos (1959) who was diagnosed as "general mucinosis". Cases of myxoedema of the skin may be divided into two groups, the pre-tibial type which is associated with an endocrine defect and a second group in which no endocrine abnormality is present. At first sight the present patient appears to be a mixture of the two, the leg lesions suggesting the former group, and the forehead lesions the latter. However, I wonder whether the lesions on the forehead may not be due to old acne scars in which for some reason mucin has been deposited. I would like to know if anyone has seen mucin deposited in scars elsewhere in patients with pre-tibial myxoedema?

REFERENCE.

DEGOS, R. (1959) *Ann. Derm. Syph., Paris*, **86**, 486.

Dr. M. A. SMITH : In a section from the forehead, the infiltration was only small compared with the legs.

Dr. I. B. SNEDDON : Recent Italian workers have shown that the skin affected by pre-tibial myxoedema contains large amounts of thyrotropin (TSH) (Baccaredda-Boy, 1959). One of the difficulties of confirming this is the lack of material. This case would certainly provide plenty.

REFERENCE.

BACCAREDDA-BOY, A. and GIACOMETTI, A. (1959) *Minerva Derm.*, **34**, 3.

Dr. P. BORRIE : There is still some doubt as to whether there are not two types of exophthalmos. The type in which pre-tibial myxoedema occurs is associated with hyperthyroidism and finger clubbing may also be seen. There is no increase in orbital tension, the substance at the back of the orbit consists of fat and areolar tissue, in serious or prolonged cases there may be atrophy of the ocular muscles and radiotherapy has no effect. The other type, malignant exophthalmos, is a pituitary manifestation and pre-tibial myxoedema does not accompany it. There is increased orbital tension, the substance at the back of the orbit is granulation tissue, there is hypertrophy rather than atrophy of the ocular muscles and the condition responds to radiotherapy. The present case fulfills all the criteria of the first type and the possibility of the existence of these two types should be born in mind when dealing with cases of pre-tibial myxoedema.

Dr. M. FEIWEL : Dr. Borrie has over-simplified the problem of exophthalmos. Sir Russell Brain (1959) concluded that, as yet, thyrotoxic or thyrotrophic exophthalmos could not be differentiated clearly on a clinical or experimental basis. When Dr. Borrie said that pre-tibial myxoedema does not occur in exophthalmos, presumably of pituitary origin, I wondered whether that was so (Freeman, 1958).

REFERENCES.

BRAIN, W. R. (1959) *Lancet*, i, 909.

FREEMAN, A. G. (1958) *Ibid.*, ii, 57.

Angiomatosis with Atrophy.—Dr. P. J. HARE.

A girl aged 14½ years.

History.—This girl was born with widespread flat angiomata, some of which have disappeared completely. On the hands, however, marks remain. There is no history of ulceration or of radiotherapy.

She was born three weeks prematurely (her mother states that all her children were born three weeks before the expected date of confinement). Her mother felt unwell during the pregnancy but had German measles at some other time. The child weighed only 3 lb. at birth ; she was not given oxygen. Although she reached the milestones of development at normal ages, she has remained small for her age. Menarche at 11 years. At school she stands 14th in a class of 28.



FIG. 1.

She does not blister abnormally easily with injury or on exposure to sunlight. Whooping cough at 3 months. Suffers from frequent colds in the winter but not subject to bronchitis. Has worn glasses since the age of 11. Four normal brothers.

Clinical findings.—Height 4 ft. 7 in., weight 5 st. 2 lb. clothed (means for age and sex 5 ft. 3 in., 8 st.). Secondary sexual features well developed. Hands small, with short tapering fingers : these are not cold or hard. No abnormality on general examination, with particular reference to cardiovascular system. The hands are radiologically normal. Urine normal.

On the forehead, cheeks, trunk, arms and legs there are scattered capillary naevi some of port-wine stain character and others telangiectatic. Mucous membranes normal. On the backs of the hands, wrists and fingers there are round depressed scars about 2-4 mm. in diameter, lying in diffusely atrophic skin (Fig. 1). At the edges of some of these areas there are traces of the angiomatous change which preceded

them. In the scalp there is a linear bald area about 2 cm. in length. The teeth and nails are normal.

Comment.—This case does not seem to resemble cases of Thomson's congenital poikiloderma in that the primary change was angiomatous. When seen at another hospital at the age of three it was said that the naevi would disappear by the age of seven. This would suggest that the original lesions were at least in part of the tuberous variety, but her mother insists that they have always been flat. Gougerot and Burnier described a child aged 16 months with a "*naevus avec points atrophiques sans ulcérations antérieures*", born with a violaceous network all over the skin, which by four months had faded on the nape, one arm and the one-half of the thorax and abdomen. A coarse network remained, particularly on the other forearm and both legs. Thereafter, spontaneous regression continued, so that at the time when the case was presented, the network was very attenuated on the arms and legs, and on the trunk there were only a few scattered patches. On the right external malleolus there was a tuberous angioma the size of a pea. On the back of the right hand and on the right knee amidst violaceous-red naevi there was pinkish-white atrophy, studded with or bordered by telangiectasis, which had appeared without previous ulceration. The child was otherwise "magnificent". A paternal uncle had an extensive vascular naevus on the back and the right arm.

REFERENCES.

- GOUGEROT, H. and BURNIER (1928) *Bull. Soc. franç. Derm. Syph.*, **35**, 804.
 THOMSON, M. S. (1936) *Brit. J. Derm.*, **48**, 221.

Hypostatic Changes Resembling Kaposi's Idiopathic Haemorrhagic Sarcoma.—Dr. BRIAN RUSSELL.

A man aged 29. Schoolteacher.

History.—Sixteen years ago itchy rash on dorsum of right foot leaving purple discoloration.

At 14 hard scaly lesions lateral aspect of right ankle.

At 15 ulceration over medial malleolus. Pain on standing.

Since : Recurrent ulceration in purple area.

At 17 biopsy—vascular stasis.

Right foot sweats more than left.

On examination.—Right foot and calf swollen. Right foot is warmer than left.

Purple, confluent scaly area on lateral aspect of ankle and dorsum of right foot with outlying slightly elevated soft nodules. Distended veins of right leg and lower thigh. Scars of ulcers. Blood pressure.: 155/70 mm. of mercury. Urine N.A.D.

Investigations.—Biopsies : 1950 : Dilated capillaries and pigmented macrophages. 1953 : Increase of capillaries in superficial dermis ; vessels normal in structure. Scanty pigment macrophages. 1959 : Hyperkeratosis. Dilatation of superficial capillaries with basophilic change in adjacent dermis. Iron pigment in dermal macrophages and in interstitial tissue of sweat glands.

Wassermann reaction negative. E.S.R. 4 mm. in 1 hour. Blood count normal.

Dr. D. I. WILLIAMS : I think this man has an extensive arteriovenous aneurysm. There is a haemangioma overlying it, more hyperkeratotic than one usually sees. The leg is larger and hotter than the other.

Addendum.—The right femoral arteriogram showed that the femoral artery is considerably larger than normal. The posterior and anterior tibial arteries are also enlarged. There is a mass of fine abnormal vessels throughout the foot, particularly around the heel and the sole. The appearances indicate diffuse arteriovenous malformation involving the subcutaneous tissues of most of the right foot.

The following cases have been published in *Proc. R. Soc. Med.*, **53**, 382.

Argyria.—Dr. A. SCOTT and Dr. P. F. BORRIE.

Chronic Lymphoedema.—Dr. P. F. BORRIE.

The following cases were also shown :

Reticulosis.—Dr. C. F. H. VICKERS (for Dr. I. B. SNEDDON).

Malabsorption Syndrome ; Lichenoid Eruption.—Dr. R. M. B. MACKENNA.

Subcorneal Pustular Dermatoses.—Dr. A. SCOTT.

Reticulosis.—Dr. N. A. SMITH.

Naevoxanthoendothelioma.—Dr. E. LIPMAN COHEN.

Psoriasis Treated with Triamcinolone and Vitamin A.—Dr. A. JARRETT.

Mycosis Fungoides.—Dr. P. HALL-SMITH.

Linear Lichen Planus, Vitiligo and Leukotrichia with a Past History of Alopecia and Morphoea.—Dr. JOHN MORGAN.

BOOK REVIEWS.

RADIOTHERAPY OF SKIN DISEASES.*

THIS most excellent volume is edited by A. Marchionini and C. G. Schirren of Munich University Skin Clinic, and, in addition to Schirren himself, there are sixteen contributors. It is intended as a supplement to the 1929 Volume V/2 on "Strahlentherapie" in Jadassohn's *Handbuch der Haut-und Geschlechtskrankheiten*. It is, however, nearly twice as big. This seems a bit anomalous, in view of the fact, as the authors recognize, that in the last few years there has been a reduction in the range of conditions considered suitable for radiotherapy, owing partly to better rival methods and partly to an increased awareness of the hazards to gonads and bone-marrow. The thirty years' interval, however, since the earlier volume, did demand substantial extension; and in part complete rearrangement, especially for the sections on the physical and biological foundations of radiotherapy. In all sections, earlier work is clearly summarized.

The material is divided into the following chapters:

Physical foundations of Dermatological X-ray Therapy and Measurement of Ionizing Rays, 80 pages.

Biological Foundations of X-ray Therapy, 95 pages.

General Methods in X-ray Treatment of Skin Diseases, 108 pages.

X-ray Treatment of Benign and Malignant Tumours of the Skin, 175 pages.

X-ray Treatment of Dermatoses other than Tumours, 135 pages.

Total Irradiation, Distant X-irradiation of the Skin and Indirect Irradiation Methods in the Management of Dermatoses, 56 pages.

Epilation Irradiation, 92 pages.

Radioactive Substances in Dermatology, 156 pages.

X-ray Diagnosis in Dermatology (with special reference to soft-ray diagnosis), 39 pages.

Irradiation Injuries and Methods of Protection, 79 pages.

Light Biology and Light Therapy, 121 pages.

Physical Treatment of Skin Diseases, 117 pages.

There follows in tabular form a translation into English, French, Spanish and Italian of terms used in radiation and other physical methods of treating skin diseases, together with explanations, 35 pages.

The chapters giving present-day views on clinical indications, technique and dosage are concise and practical and, if published separately and at a moderate price, would make a manual which every dermatologist and dermatological radiotherapist would do well to acquire.

With regard to gonadal and haematological hazards, these must not be exaggerated, especially if one chooses suitable qualities. The German school was early in recognizing the appropriateness of softer rays in dermatology—a view which is happily gaining acceptance. As "dermatological universal apparatus", machines with beryllium tube energized from 10 to 50 (more seldom to 100) kV. are advocated. As a general guide (but not without exception), the H.V.D. (half value depth in tissue) should equal the depth of the base of the lesion.

I have nothing but praise for this important work, which is beautifully and accurately produced.

W. N. G.

* *Strahlentherapie von Hautkrankheiten*. (1959). Ed. by A. MARCHIONINI and C. G. SCHIRREN. Berlin: Springer. Pp. 1394, 662 black and white and coloured illustrations. Price DM. 460.

CUTANEOUS MANIFESTATIONS OF THE MALIGNANT LYMPHOMAS.*

THE author divides his subject into three main parts, mycosis fungoides, Hodgkin's disease and lymphosarcoma. He discusses each in detail under numerous sub-headings including aetiology, pathogenesis, symptoms, cutaneous lesions, differential diagnosis and treatment. To the dermatologist, mycosis fungoides is the most important of these diseases and we find 210 pages devoted to it and over 400 references. The author believes that mycosis fungoides is a disease in its own right, with a distinctive histology, but that the name should be reserved for cases showing the classical picture as seen by the dermatologist. The *tumeur d'emblée* and erythrodermic variants should be excluded. He believes the *d'emblée* cases are due to lymphosarcoma whilst the erythrodermic forms are manifestations of lymphocytic leukaemia, Hodgkin's disease, or some other kind of malignancy, but not mycosis fungoides.

The book is well printed and includes good illustrations. It is a valuable work to consult but the frequent references to the literature make it difficult to read in places.

P. D. S.

RADIOTHERAPY.†

THIS is the second edition of a book first published in 1950. It deals with the physical properties and biological effects of ionising radiation, the history of radio-therapy, radiation hazards, the duties and responsibilities of radiotherapists, the principles of treatment and dosage, and the techniques used in malignant and non-malignant cases.

The single dose method is regarded as convenient for some rodent ulcers but the cosmetic results are not so good as when the dose is fractionated. There is also an increased risk of late necrosis. A course of 500 rads daily for 9 or 10 exposures is recommended.

With Grenz rays the depth dose is 4 per cent at 2 mm. and the authors state that it is difficult or impossible to cause serious skin damage, late cancer production being unknown and there being no risk of epilation or of damage to underlying structures such as the eyes, testes, or epiphyses. Early basal cell carcinomas respond to Grenz therapy.

The use of thorium-X is mentioned but there is no indication of any possible hazard to the therapist from inhalation.

In the treatment of dermatosis of the hands it is emphasized that at 2 cm. and 100 kV. the exit dose is 40%, from which it follows that 71 rads given to each surface has the effect of 100 rads on each surface. The authors apply the general rule that a total dosage of 1000 rads given over several years should not be exceeded to any but a tiny area.

There are five pages on the treatment of tinea capitis by epilation, a treatment which may now fortunately have passed into the dusty files of history.

In the treatment of simple haemangioma it is recommended that 300–800 rads be given, "the treatment beginning as early as possible, to prevent enlargement". But on p. 460 there are excellent photographs of spontaneous resolution and the authors add that "it is generally safe and wise to leave them alone". The chief indications for treatment are medical, for example, feeding difficulties or psychological reasons "to appease a distracted parent who will not be reassured". But there are simpler

* *Cutaneous Manifestations of the Malignant Lymphomas*. SAMUEL M. BLUEFARB (1959) Springfield: Charles C. Thomas. Oxford: Blackwell Scientific Publications. Pp. 534. Illus. 47 half-tone and 1 colour. Price £6 4s.

† *A Short Textbook of Radiotherapy*. J. WALTER and H. MILLER (1959). London: J. and A. Churchill Ltd., 2nd Ed. Pp. 527. Illus. 303. Price 56s.

innocuous placebos for this purpose. Happily there is no enthusiasm for radiotherapy in the treatment of plantar warts.

This dermatological section is incomplete and not always precise. Malignant melanoma is described as synonymous with melanocarcinoma or melanosarcoma. There is no mention of molluscum sebaceum, nor of cutaneous reticulosos excepting Hodgkin's disease and lymphosarcoma. It is a little startling to hear that "barber's rash is the same condition as sycosis barbae since the infection is often acquired at the barber's". Surely epilation is rarely needed to-day in this condition.

This book can be recommended for authoritative reference as to the basic facts of irradiation, but many dermatologists would not agree with some of the opinions expressed in the shrinking field of dermatological radiotherapy.

B. F. R.

ROENTGENOLOGY.*

THE statement on the dust cover that "there is nothing like this on the market today" is probably correct. This book aims "to present in a short succinct fashion the scope of roentgenology as it applies to skin disorders". The author states that he is not an expert in the physics of radiology, and believes that this is not necessary for a dermatologist who practises radiotherapy. The physics given in the book, however, is mainly correct, but inadequate for reference. Inaccuracies do occur e.g. Figs. 2 and 3 are incorrect. On page 1 we read that a charge essentially without mass is an electron. Five lines later we read that an electron has a "mass about 1/1800 of a hydrogen atom".

The book lays itself open to criticism as the treatment of malignant cutaneous neoplasms (perhaps with the exception of rodent ulcers) is better carried out by specialist radiotherapists in consultation with dermatologists. From a clinical point of view there is much to disagree with. The natural history of strawberry naevi should be well known to all doctors, and radiotherapy is not only usually superfluous but sometimes harmful. *Microsporium canis* ringworm infection of the scalp should not be treated as a routine by x-ray epilation (thus applied even before the advent of griseofulvin). It is not clear what the author means by "fairly young keloids" and he does not distinguish between basal and squamous cell carcinomas, calling them loosely epitheliomas. The statement that the scalp should not receive more than 150r per month might be most misleading. X-ray treatment is recommended for leukoplakia. Treatment for plantar warts is rather like a double-barrelled shotgun: 1000 to 3000r units followed by the use of salicylic acid plasters!

O. L. S. S.

* *X-ray and Radium in Dermatology*. B. A. WANSKER (1959). Springfield: Charles C. Thomas. Pp. 114. Price 37s. 6d.

INTERNATIONAL CONGRESS OF DERMATOLOGY 1962.

THE organizers of the International Congress of Dermatology to be held in Washington D.C. in September 1962, propose that in addition to the usual "live" case presentations, others might be made through the medium of colour cinematography. Anyone who is interested in presenting films at the meeting should write to Dr. G. B. Mitchell Heggs at 56 Gower Street, London, W.C.1.

CURRENT LITERATURE.

DIFFERENTIAL DIAGNOSIS OF ERYTHEMA INDURATUM BAZIN. K. HEKELE and O. LOFFERER. (1959) *Derm. Wschr.*, 139, 650.

Occasionally difficulties arise in the differential diagnosis of Bazin's disease and the follicular, papular and nodose type of *Trichophyton rubrum* infections of the calf. Fungus should be easily identifiable in most cases, but if difficulty is encountered then an occlusive dressing with adhesive or Unna's paste for a few days will prove to be helpful. Section may show hyphae or be inconclusive.

J. M.

MYOBLASTOMA OF THE TONGUE. X. VILANOVA and C. CARDENAL. *Actas Dermo-Sif., Madrid*, 50, 68.

A case of granular-cell myoblastoma of the tongue is described in a man aged 37. The middle and deep dermal layers contained granular foamy myoblasts—round or elongated cells the granules of which stained yellowish with Sudan III. The authors review the various theories of origin of these tumours of which over 300 had been described up to 1950. From the histological study of their case they find no support for regarding its origin as muscular injury or that it is a tumour of nerve elements. They also consider a naevoid origin unlikely.

P. I.

COMMENTARY ON THE TREATMENT OF PSORIASIS. ENRIQUE ALVAREZ SAINZ DE AJA. *Actas Dermo-Sif., Madrid*, 50, 83.

The author accepts the importance of emotional factors in determining attacks of psoriasis as in other cutaneous reactions but he knows of no cases of psoriasis in which the psychosomatic approach alone has been curative. He believes that the primary cause of psoriasis is not in the skin but that there is an unknown link relating the skin in psoriasis to rheumatism, septic foci, endocrine and other disorders. Simple chemical effective agents in treatment are coal tar, pyrogalllic acid and chrysarobin. But general remedies of value are sodium salicylate and intra-muscular injections of Enesol three times weekly. He finds gold salts occasionally successful and frequently staphylococcal toxoid gains striking successes. On the other hand he has seen no benefit from E.C.T., bromides, psychoanalysis or modern diuretics. Although cortisone-like drugs may give remission the clinical picture is unaltered or worse after their withdrawal—leaving disillusionment and financial impoverishment in their wake. He finds thiosemicarbazone worth a trial but has not been encouraged by digitalis, barbiturates, chlorpromazine or reserpine.

P. I.

GIANT PRICKLE CELLED EPITHELIOMA. G. JAQUETI DEL POZO and R. GARCIA MONTELONGO. *Actas Dermo-Sif., Madrid*, 50, 87.

The authors describe an enormous epithelioma 8 cm. in diameter on the left cheek of a woman aged 73. They cured it by a combination of electrocoagulation and radiation by contact therapy of the Chaoul type. They believe very large epitheliomas are best treated by using separate small fields of irradiation not exceeding 4 cm.

P. I.

TREATMENT OF DERMATITIS HERPETIFORMIS AND HERPES GESTATIONIS WITH SULPHAMETHOXYPYRIDAZINE. X. VILANOVA and J. M. DE MORAGAS. *Actas Dermo-Sif., Madrid*, 50, 439.

Four cases of dermatitis herpetiformis in females between the ages of 54 and 70 were satisfactorily controlled by the drug, the required dosage varying between 0.1 and 0.5 g. daily. One case of herpes gestationis commencing one month before a third parturition and with post-partum aggravation is described. 15 mg. of prednisone daily failed to control the eruption but it responded to sulphamethoxypyridazine. Ten weeks after delivery the eruption did not re-appear when the drug was stopped.

A woman aged 68 had an 11 months' history of an atypical eruption of erythemato-pustular elements and blisters—which were sub-epidermal and very itchy and involved the mouth extensively. This eruption responded poorly to a first course of the drug and a second course was

followed by a violent exacerbation with large bullae and fever which the authors consider drug-induced. P. I.

STATISTICAL STUDY OF 141 CASES OF PAPULAR URTICARIA FROM BARCELONA UNIVERSITY SKIN SERVICE. X. VILANOVA and J. M. CAPDEVILA. *Actas Dermo-Sif., Madrid*, 50, 357.

One hundred and forty-one cases of papular urticaria were seen, 69 (48.9%) of which did not return for follow up possibly owing to the transitory nature of their attacks. The 72 others were classified aetiologically as follows:

1. One long lasting case in a boy aged 5 was considered due to vitamin F deficiency as a result of fat, cholesterol and iodine investigations.
2. Eighteen cases (25%) were due to intestinal parasites (chiefly thread worms, but also round worms and *Trichocephalus latus*).
3. One case was due to pediculosis corporis.
4. Fourteen cases (19.5%) to feeding faults (irregular meals at too frequent intervals, excess of carbohydrates, starchy foods and chocolate). This group was treated by general dietetic advice only.
5. Twenty-five cases (35%) were considered to be hypersensitive to their intestinal organisms. Positive skin tests were obtained to dilutions of these organisms (especially *B. coli*, proteus and various types of streptococci). Treatment of this group was for one week only by poorly absorbed sulphonamides (phthalyl sulphathiazole, formol sulphamido sulphathiazole, sulphaguanidine). Doses were only 0.5 g. t.i.d. The second week's treatment was intestinal ferments only. Results in this group are recorded as spectacular and only one case required a second course of intestinal ferments to establish a permanent and adequate flora.
6. In 13 (18%) no cause was found and diathesis blamed. Treatment of these was by pyridoxine, whole vitamins and calomel twice weekly. P. I.

ADVANCES IN THE TREATMENT OF SKIN DISEASES. P. BORRIE. (1959) *Practitioner*, 183, 419.

Among recent introductions, trimeprazine is mentioned as an antipruritic. Triamcinolone may be invaluable in erythrodermic psoriasis, but in chronic discoid psoriasis, although approximately 60% of cases respond, the malady invariably returns when the drug is withdrawn, sometimes as a severe exacerbation. In exfoliative dermatitis and pemphigus vulgaris, cases which are not responding to routine steroid therapy occasionally show remarkable improvement with triamcinolone.

For topical therapy, neomycin is advised as the first choice against staphylococci, and polymyxin should be used in the presence of *Pseudomonas pyocyanea*. Nystatin ointment is recommended for local applications in cases of chronic monilial paronychia. R. J. C.

ADVANCES IN THE TREATMENT OF LEPROSY. R. G. COCHRANE. (1959) *Practitioner*, 183, 483.

An excellent review of modern therapy in leprosy, including sulphones, diphenyl thiourea and ditophal ("Etisul"). R. J. C.

TREATMENT OF KAPOSI'S SARCOMA OF THE LOWER EXTREMITY BY EXTRACORPOREAL PERFUSION WITH CHEMOTHERAPEUTIC AGENTS. A. P. MONACO and W. G. AUSTEN. (1959) *New Engl. J. Med.*, 261, 1045.

A new technique for treating Kaposi's haemorrhagic sarcoma with nitrogen mustard is described. The aim of the method is to supply the greatest possible amount of nitrogen mustard to the diseased area without the usual risks to the gastro-intestinal tract and haemopoietic system.

This is accomplished by regional perfusion with an extracorporeal circuit. Details of two patients who benefited by this procedure are given. A. D. P.

ERYTHEMA MULTIFORME ASSOCIATED WITH SULFAMETHOXYPYRIDAZINE ADMINISTRATION. R. C. GARVER. (1959) *New Engl. J. Med.*, 261, 1173.

The appearance of Stevens-Johnson syndrome in three children who had taken sulfamethoxy-pyridazine is described. A. D. P.

SARCOIDOSIS AND HYPERPARATHYROIDISM WITH HYPERCALCEMIA: SPECIAL USEFULNESS OF THE CORTISONE TEST. J. M. BURR, J. J. FARRELL and A. G. HILLS. (1960) *New Engl. J. Med.*, 261, 1271.

When calcium in the blood is abnormally high in sarcoidosis the level can be reduced by cortisone, but this does not happen when the cause is hyperparathyroidism. By giving cortisone to a woman with hyperparathyroidism and sarcoidosis the authors were able to show that hypercalcaemia in her case was caused by hyperparathyroidism and was not the result of sarcoidosis. A parathyroid tumour was successfully removed.

A. D. P.

TUBEROUS SCLEROSIS: GENETIC DOMINANCE. D. MARSHALL, G. B. SAUL and E. SACHS. (1959) *New Engl. J. Med.*, 261, 1102.

The occurrence of tuberous sclerosis in two families was investigated and is recorded in their trees. The mode of inheritance is shown to be by a dominant gene which can be affected by a pair of modifying genes.

A. D. P.

PHOTOSENSITIVITY DUE TO CHLOROTHIAZIDE AND HYDROCHLOROTHIAZIDE. L. C. HARBER, A. M. LASHINSKY and R. L. BAER. (1960) *New Engl. J. Med.*, 261, 1378.

Photosensitivity in four women taking chlorothiazide or hydrochlorothiazide is reported. Tests with filters showed the action spectrum to lie between 2750 Å and 3100 Å. It is suggested that the reaction was due to a photoallergic rather than a phototoxic mechanism.

A. D. P.

GRISEOFULVIN IN THE DEEPER CUTANEOUS MYCOSES. F. LATAPI, P. LAVALLE, J. NOVALES and Y. ORTIZ. (1959) *Dermatologia, Mexico*, 3, 34.

Actinomycosis of one foot that had been present for 3 years but had not affected the bones was treated with griseofulvin, 1 g. daily. After four days the lesions were noticeably flatter and at the end of a month there seemed to be a clinical cure; but on lifting up a few tiny crusts there were found small drops of pus which contained microscopic "granules" and from which *N. brasiliensis* was again cultured.

From a 3-month-old lesion on the cheek of a child aged 3 *Sporotrichum schenckii* was cultured. The skin, when tested with sporothricin gave a strong positive reaction after 48 hours. Clinically the lesions were cured after 4 weeks' treatment with griseofulvin.

G. W. B.

THRESHOLD STIMULATION OF THE SKIN AND HOUSEWIVES' ECZEMA OF THE HANDS.

HARRY SIGEL. (1959) *Arch. Derm., Chicago*, 80, 461.

The mechanism of housewives' eczema can be explained as a combination of thin epidermis and repeated exposure to mild primary irritants. The thickness of the epidermis was judged by degree of response to chemical (cantharides) and electrical stimulation.

J. K.

INTERMEDIARY METABOLISM OF PHENYLALANINE AND TYROSINE IN DIFFUSE COLLAGEN DISEASE. II. INFLUENCES OF LOW PHENYLALANINE AND TYROSINE DIET UPON PATIENTS WITH DIFFUSE COLLAGEN DISEASE. N. NISHIMURA, H. OKAMOTO, M. TASUI, K. MAEDA and K. OGURA. (1959) *Arch. Derm., Chicago*, 80, 466.

Patients with rheumatoid arthritis, chronic discoid L.E., acrosclerosis, generalized scleroderma or dermatomyositis were treated with low phenylalanine and tyrosine diet with improvement and no serious side effect. When this diet was used for dermatomyositis along with cortisone half the usual dose of cortisone was sufficient and the effect lasted longer.

J. K.

SENILE PURPURA AND LIVER DISEASE. VINCENT J. DERBES and MARVIN E. CHERNOSKY (1959) *Arch. Derm., Chicago*, 80, 529.

In 10 patients with senile purpura, needle biopsy of the liver showed abnormal findings in 9. It is considered that the presence of senile purpura warrants investigation of liver function.

J. K.

VISUAL DISTURBANCES WITH ANTIMALARIAL DRUGS, WITH PARTICULAR REFERENCE TO CHLOROQUIN KERATOPATHY. H. E. HOBBS and C. B. CALNAN. (1959) *Arch. Derm., Chicago*, 80, 557.

Corneal changes occur in an unknown proportion of patients treated with antimalarial drugs. There are two varieties of change, one, transient oedema, a toxic manifestation in susceptible

subjects, and the other an insidious deposit of an opaque substance in the cornea of more substantial duration. High dosage increases the risk and more serious and permanent retinal changes may occur. J. K.

MULTIPLE ECZEMATOUS SENSITIVITIES. R. L. BAER. (1959) *J. Amer. med. Ass.*, **170**, 1041.

Three kinds of eczematous "sensitivity" are discussed here:

- (i) The subject has a low threshold to primary irritants which results in multiple non-specific eczematous reactions;
- (ii) the subject acquires multiple specific allergic sensitivities to chemically unrelated substances; and
- (iii) the subject shows a specific allergic sensitivity to contact with one substance and then allergic reactions to chemically related substances (cross-sensitization). G. C. W.

ERYTHEMA NODOSUM AS A MANIFESTATION OF HISTOPLASMOSIS. S. SASLAW and F. M. BEMAN. (1959) *J. Amer. med. Ass.*, **170**, 1178.

A Danish girl was tuberculin-positive and histoplasmin-negative on arrival in the U.S.A. (Ohio), and 3 months later she developed erythema nodosum with malaise, pneumonitis and hilar adenopathy. The histoplasmin test had become positive and the illness (including the erythema nodosum) was attributable to recent histoplasmosis. G. C. W.

METHYLPREDNISOLONE IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS. E. L. DUBOIS. (1959) *J. Amer. med. Ass.*, **170**, 1537.

Forty patients with systemic L.E. were treated with methylprednisolone and the response was comparable to that which occurs with other steroids. It ranked as 1.1 times as effective as prednisone. Most of the side effects were met with to the same extent as with other steroids though diabetes did not occur in this series. New peptic ulcer occurred in 5%. Ecchymoses were much commoner and 27% of patients showed them. G. C. W.

FINGER TIP HYPERAESTHESIA. W. B. SHELLEY and D. M. PILLSBURY. (1959) *J. Amer. med. Ass.*, **170**, 1779.

Punctate hyperaesthesia of the finger tips in a hairdresser was traced to penetration of the epidermis by tiny particles of silica from a new type of hair curler. G. C. W.

CYSTIC FIBROSIS IN ADULTS WITH A STUDY OF SWEAT ELECTROLYTE VALUES. E. M. PETERSON. (1959) *J. Amer. med. Ass.*, **171**, 1.

In children with fibrocystic disease a high concentration of sodium chloride in sweat is diagnostically important. On applying the sweat electrolyte test to 262 adults, 14 were found to show a high figure and most of these had bronchiectasis. In these cases a mild degree of fibrocystic disease seemed probable. G. C. W.

HERPES ZOSTER IN CHILDREN. R. K. WINKELMANN and H. O. PERRY. (1959) *J. Amer. med. Ass.*, **171**, 876.

Seven cases of herpes zoster are described here in children between the ages of 7 months and 5 years. Five of them had had varicella during the first year of life. In these seven cases the course of the herpes zoster was short and mild, though pain, fever and general irritability were often present. One child had a meningitic reaction. No child had post-herpetic pain. G. C. W.

NEW CLINICAL CONCEPT OF SYSTEMIC LUPUS ERYTHEMATOSUS. C. E. RUPE and S. N. NICKEL. (1959) *J. Amer. med. Ass.*, **171**, 1055.

An analysis of 100 cases of systemic lupus erythematosus from the Henry Ford Hospital in Detroit. There is little detailed information on the cases, and much discussion out of which emerges the "new concept", namely that systemic lupus erythematosus is not always such a severe disease as it was at one time thought to be. G. C. W.

PROBLEMS AND TREATMENT OF THE CIRCUMILEOSTOMY SKIN. R. J. McNAMARA, E. M. FARBER and S. I. ROLAND. (1959) *J. Amer. med. Ass.*, **171**, 1066.

The information discussed here is based on 451 replies from letters to people in U.S.A. and Great Britain with ileostomies (nearly all with ulcerative colitis). Seventy-six per cent of these patients said that they had had trouble with the skin round the ileostomy stoma, most commonly in the 6 weeks following operation. The management and treatment of the skin round the stoma is discussed.

G. C. W.

OBSERVATIONS ON GRENZ RAY REACTIONS. F. KATZ. (1959) *Dermatologica, Basel*, **118**, 357.

This careful study includes the following up of many patients, after many years. Katz distinguishes four erythema "cycles". The first wave appears within a few hours after an application of 1080 r to 1440 r, at HVL 0.02 mm. Al, and fades quickly. The second wave reaches its peak between the 10th and 14th days and lasts 3 or 4 days. The third, and most intense erythema, which he calls the "main erythema", occurs between the 24th and 34th days, and lasts for 5 to 7 days. This main erythema occurs only when individual doses were 400 r or more, and only in cases where it did occur were slight signs of damage seen, years later. He believes that as much as 1200 r a year for ten years in succession can be given with complete safety, if the individual doses are never greater than 100 r or 150 r. He records apparently the first case in the literature of squamous carcinoma from overdosage of Grenz rays, on the finger of a physician who had worked for many years with these rays, and whose skin showed signs of gross overdosage.

J. F. S.

MALIGNANT SCLERODERMIA. Z. ŠTAVA. (1959) *Dermatologica, Basel*, **118**, 371.

An account of five cases of fatal generalized sclerodermia. The author uses the term "malignant" not as meaning a new disease, but to emphasize that generalized sclerodermia can end fatally, sometimes within a few months. The disease is truly general, involving viscera as well as skin. Raynaud's phenomenon was in no case an early symptom, and might never appear. It never preceded sclerosis, as it does in typical acrosclerosis. Serum protein is low; gammaglobulin high, though less so than in extensive acrosclerosis. Three cases suggested rheumatoid arthritis, one acute i.e., while the fifth showed a severe haemorrhagic diathesis. The conclusion is that these cases represent a stereotyped cutaneous reaction to various primary noxae.

J. F. S.

EXPERIMENTS IN BLISTER FORMATION. J. P. E. BURBACH. (1959) *Dermatologica, Basel*, **118**, 379.

Specimens of living human skin were injected with active enzyme solutions: trypsin and hyaluronidase solutions and proteolytically active epidermal extracts, by a method evolved by the author. It was found that trypsin solutions, dependent on concentration and period of application, were capable of breaking up the connection between epidermis and corium, and between the cells of the epidermis itself. No such changes were brought about by the hyaluronidase solutions used. No differences were seen between the two kinds of hyaluronidase.

In experiments with epidermal extracts, no difference was found in degree of detachment between proteolytically active extracts and solvents only. Skin from autopsy differed in that it resisted the action of some solvents. In two cases detachment of epidermis from corium was produced in autopsy skin by injecting an active epidermal extract, whereas controls injected with the buffer solution showed no changes.

A sub-epidermal vesicle could be produced in a living subject by injecting a trypsin solution of a certain concentration.

(Slightly modified from author's summary.)

J. F. S.

THE TREATMENT OF PARAPSORIASIS VARIOLIFORMIS WITH ACRIDINE AND QUINOLINE DERIVATIVES. E. NAGY and E. BALOGH. (1959) *Dermatologica, Basel*, **118**, 391.

Of three patients treated with Atebrine or Resochin, two recovered completely, while the third was improved.

J. F. S.

"COLLODIUM BABIES". E. H. HERMANS. (1959) *Dermatologica, Basel*, **119**, 164.

A description of nine cases of this peculiar variety of Brocq's ichthyosiform erythrodermia, with a very full discussion and citation of the literature. Three of these cases occurred in one

family; there were two families with two cases each; and two cases occurring singly. While the author does not really like the name, he does not see any better alternative at the moment.
J. F. S.

DESENSITIZATION IN EXPERIMENTAL ECZEMA OF GUINEA-PIGS. W. JADASSOHN, R. BRUN and EUG. BUGARD. (1959) *Dermatologica, Basel*, **119**, 186.

The problem of desensitization in human eczema is very complex, but it is no longer possible to hold that supersensitivity, once acquired, always lasts for life. Some have thought that if a sensitive person rigorously avoided further contact with the sensitizing agent, his skin-sensitivity would decline over months or years, but the authors suggest that the avoidance in such cases is not really absolute, and that subminimal exposures have desensitized. They report success in desensitizing guinea-pigs, previously made supersensitive to dinitrochlorobenzene (DNCB) by application of very dilute (1 in 1000) DNCB in acetone. It took 100 days to produce this result, and they do not know how long it would take in man. They had no such success with other eczematogens than DNCB.
J. F. S.

A CASE OF TINEA IMBRICATA IN A WHITE BOY, TREATED WITH GRISEOFULVIN. J. C. BELISARIO and M. T. HAVYATT. (1959) *Dermatologica, Basel*, **119**, 158.

An Australian boy aged 15 acquired tinea imbricata in Fiji, and the eruption resisted a great variety of external applications. Griseofulvin, 0.25 g., four times a day at first, then stepped up to 0.5 three times a day, was rapidly successful. After eight days, and a total of 11.5 g. of griseofulvin, he was completely cured. A footnote states that four weeks later he had a slight recurrence, ascribed to incomplete sterilization of clothing, and that this yielded to a further fortnight's treatment. *Trichophyton concentricum* was demonstrated microscopically and by culture. The authors believe this to be the first reported case of cure of this very rebellious infection by oral therapy.
J. F. S.

GRISEOFULVIN. J. ESTEVES and H. NEVES. (1959) *Dermatologica, Basel*, **119**, 148.

This account from Portugal of the successful use of griseofulvin in various dermatomycoses confirms the experiences of many workers in many lands, but what is new, and rather disconcerting, is the authors' demonstration that experimental inoculation of patients' own dermatophytes on to their glabrous skin, while they were taking the remedy, produced lesions which differed from those produced in untreated controls neither in length of incubation-period, frequency of "take", clinical appearance nor course. This is directly contrary to what has been found in experimental animals (see Abstract of paper by Frey and Geleick).
J. F. S.

THE ACTION OF GRISEOFULVIN IN EXPERIMENTAL RINGWORM OF THE GUINEA-PIG. J. R. FREY and H. GELEICK. (1959) *Dermatologica, Basel*, **119**, 197.

(i) Orally administered griseofulvin, when given in a therapeutic trial, is capable of diminishing the macroscopic alterations of experimental trichophyta in the guinea-pig and of shortening considerably its fungus-positive phase. When griseofulvin is given prophylactically, the infection is completely suppressed.

(ii) Periodical examination of hairs taken from the mycotic foci shows that four days after starting treatment, i.e., on the seventh day after infection, three to four times fewer infected hairs are found in treated as compared with untreated animals.

(iii) Griseofulvin seems to act especially upon the peripillary and intracortical hyphae located near the hair-root. By this means, the proximal growth of these fungal elements is inhibited, so that as the hair grows they are shifted towards the surface.

(iv) Griseofulvin is probably incorporated in the cells of the hair-matrix, the hair-shaft and the inner hair-root, and acts on the fungal elements there.

(Modified from Authors' summary.)

J. F. S.

THE SEBACEOUS FILM IN HEALTHY SUBJECTS, EPILEPTICS AND SUFFERERS FROM PARKINSONISM. N. GRASSET and R. BRUN. (1959) *Dermatologica, Basel*, **119**, 232.

Using their own method, in which filter-paper is applied to the area of skin to be tested, stained with osmic acid vapour and examined photo-electrically, the authors show that, age for age, epileptics and the subjects of Parkinsonism excrete more sebum than do normal controls.

J. F. S.